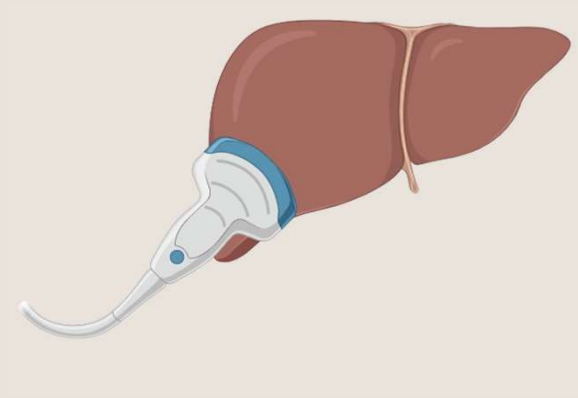
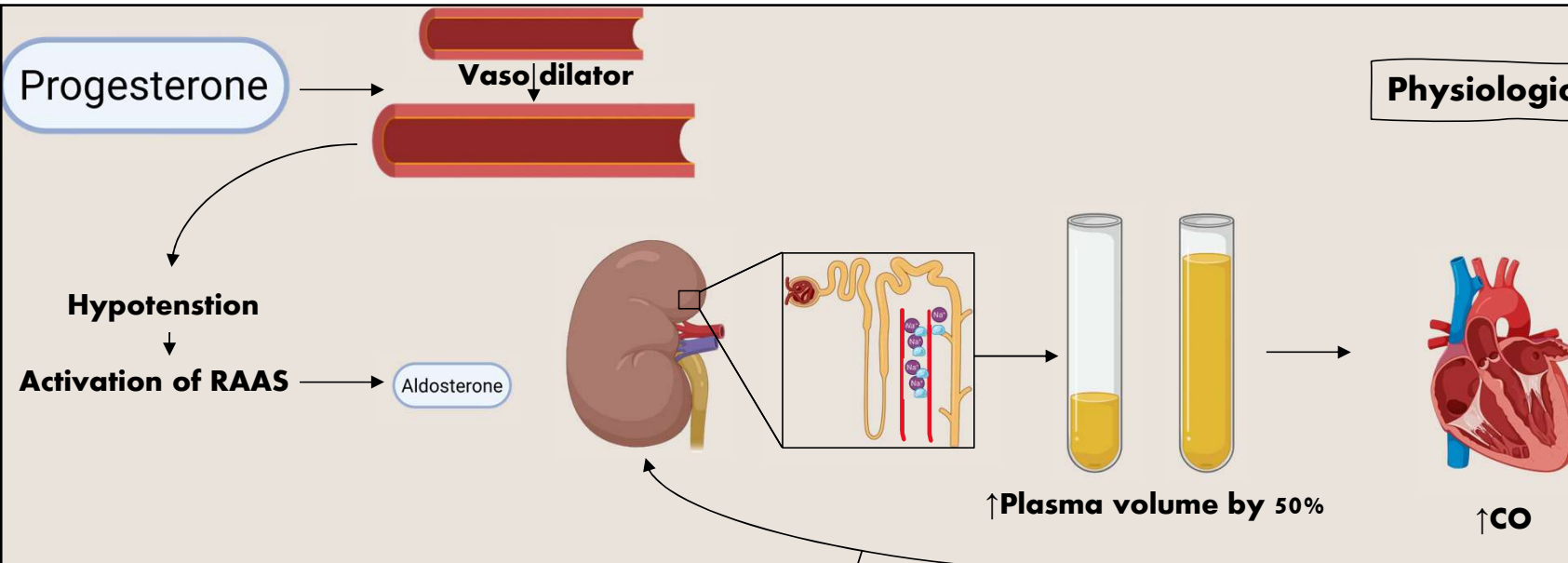


Hepatic disorders in pregnancy



**Zaid Awad
Nagd Al_qatameen
Tasneem Al_qawasmeh**

Physiological changes During Pregnancy



$$\downarrow Hct = \frac{RBC\ Volume \uparrow}{Plasma\ Volume \upupup}$$

ALT & AST remain within the **normal** range
So they can be use for detecting liver injury.

Bilirubin may **decrease** due to hemodilution.
So always in pregnancy don't forget about **hemodilution**

Pregnancy is Hypercoagulable State
To decreses risk of PPH
But this increase of VTE

- ↑ Coagulation Factor (1752/8/12)
- ↑ Fibrinogen
- ↑ Resistant to protein C / ↓ Protein S (Natural anti-coagulant)

ALP increase in third trimester due to increase in placental and bone isoenzyme.
So how to know if this increase normally due to pregnancy or pathologically ??
Gamma-glutamyl transferase can be used to confirm hepatic origin of raised ALP.



Spider nevi (aka: spider angiomas)

Central red spot and radiating thin vessels,
usually located in the trunk/ face

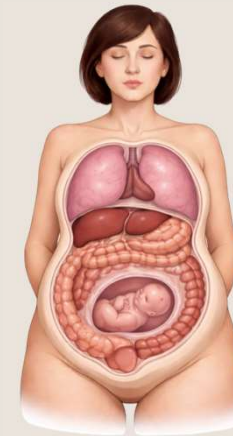
Due to **hyperestrogenemia**

- Normally in male → up to 2
 - Normally in non-pregnant → up to 5
 - Normally in pregnant → up to 10
- More than that indicate liver disease**



Palmer erythema

Usual finding in pregnancy



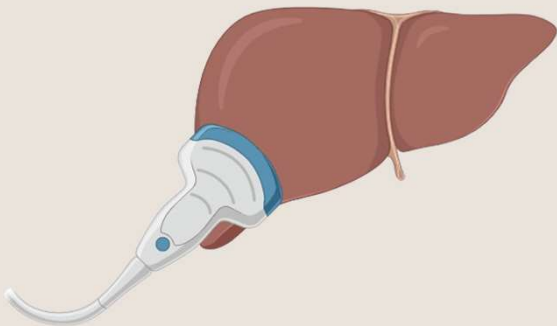
Normal liver not palpable in
healthy non pregnant female

You may just feel liver edge with fully inspiration

So in pregnancy with enlarged uterus

→ push the liver upward

→ **not palpable**



- No change in liver structure
- **Biliary sludge** found in 1/3 of pregnancy
(asymptomatic / Spontaneous resolve)
 - **Gallstone** in 2-12%

**Physical Examination & Ultrasound
finding related to Liver
In normal healthy pregnant**

Hepatic disorders in pregnancy

Trimester	Pre-existing underlying liver diseases	Liver diseases related to pregnancy	Coincidental liver diseases
First	<ul style="list-style-type: none"> • Chronic hepatitis B, C • Autoimmune hepatitis • Wilson's disease • Primary biliary cirrhosis • Primary sclerosing cholangitis • Cirrhosis of any cause 	<ul style="list-style-type: none"> • Hyperemesis, may persist in 2nd, 3rd 	<ul style="list-style-type: none"> • Acute viral hepatitis (HEV, HAV) • Gallstones • Budd-Chiari syndrome • Drug induced hepatotoxicity • Sepsis (ANY TRIMESTER)
Second		<ul style="list-style-type: none"> • Preeclampsia • ICP (late 2nd) 	
Third		<ul style="list-style-type: none"> • ICP (early 3rd) • Acute fatty liver • Pre-eclampsia, eclampsia, HELLP syndrome 	

Intrahepatic cholestasis of pregnancy (ICP)

It is characterized by **pruritus without rash** and **↑ in serum bile acid** concentration typically developing in the **late 2nd or 3rd trimester** and rapidly resolving after delivery.

So the criteria to diagnose
 1- pruritus without rash
 2- ↑ bile acid

ICP is the Most common pregnancy-specific liver disease
 Incidence of ICP: 0.2–2%
 Pruritus in pregnancy: 20%

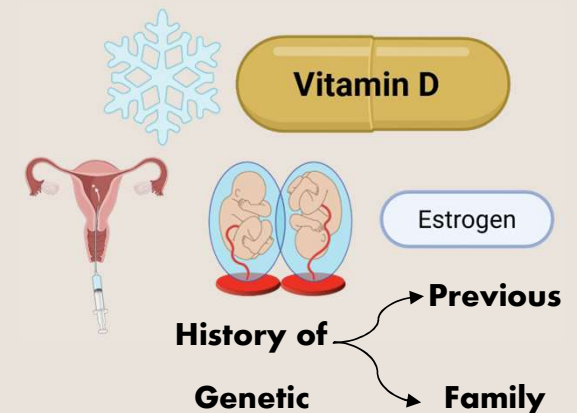
TABLE 1 Terminology for pregnant women with itching of normal skin

Diagnosis	Clinical features
Gestational pruritus	Itching and peak bile acid concentrations <19 micromol/L ^a
Mild ICP	Itching and raised peak bile acid concentrations 19–39 micromol/L
Moderate ICP	Itching and raised peak bile acid concentrations 40–99 micromol/L
Severe ICP	Itching and raised peak bile acid concentrations ≥100 micromol/L

Risk Factor



- ↑ in winter due to ↓ Vit D
- ↑ in IVF Vs Spontaneous Pregnancy (2.7 vs 2.0%)
- Multiple pregnancies
- Level of Estrogen Increase in 3rd trimester and Multiple pregnancy
- Previous Hx of ICP (90%)
- Family Hx of ICP
- Genetic → ABC4 mutation → coding MDR3 protein



History



Pruritus without rash starts on palms/soles, spreads to trunk and face

Worse at night



N/V, steatorrhea



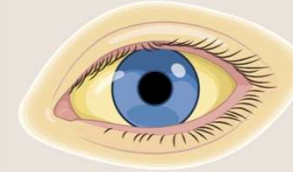
right upper quadrant pain

sleep disturbance

Examination



No primary skin lesions, but scratch marks may be appeared



Jaundice in 14–25% of cases, 1–4 weeks after onset of itching

Investigations

Bile acids: often the first and only abnormality

• **Other abnormalities:**

- **Serum aminotransferases:** elevated in 60%
- **Alkaline phosphatase (AP):** up to 4^x; not diagnostic in pregnancy
- **Total/direct bilirubin:** elevated in 25%
- **Prothrombin time:** usually normal; prolonged → Vitamin K deficiency



Differential Diagnosis

Pruritus

- **Pregnancy-specific:**
 - Pruritus gravidarum
 - Atopic eruption of pregnancy
 - Pemphigoid gestations
 - Prurigo of pregnancy
- **Preexisting causes:**
 - Atopic dermatitis
 - Allergic/drug reaction
 - Systemic disease

Abnormal Liver Function

- **Pregnancy-specific:**
 - Acute fatty liver
 - HELLP Syndrom
 - Hyperemesis gravidarum
- **Preexisting:**
 - Viral hepatitis
 - Autoimmune hepatitis
 - Veno-occlusive disease



Complications



Maternal Complications

- Increased risk of **pre-eclampsia and gestational diabetes** → monitor BP, urine, and glucose
- No evidence of increased risk of postpartum hemorrhage in uncomplicated ICP

Fetal complication

- **stillbirth, meconium-stained amniotic fluid, preterm delivery, neonatal RDS**
- fetal death may be due to **arrhythmias or placental vasospasm** from high bile acids



Risk stillbirth by Bile Acid Levels

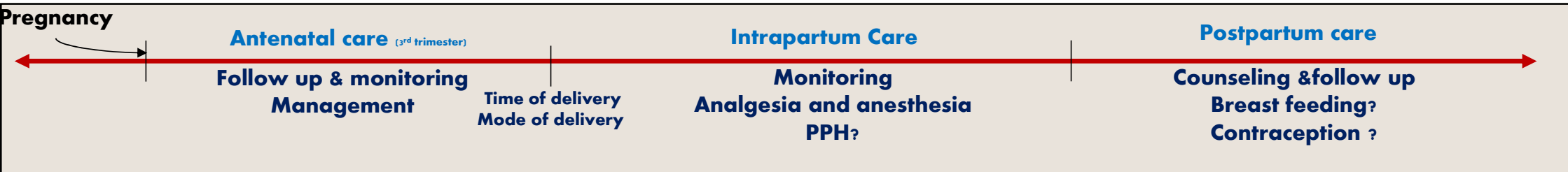
- 19–39 $\mu\text{mol/L}$: risk of stillbirth **similar to background**
- 40–99 $\mu\text{mol/L}$: risk **similar** until **38–39 weeks** gestation
- ≥ 100 $\mu\text{mol/L}$: risk **higher** than background **consider birth at 35-36 weeks** gestation

Comorbidities

Gestational diabetes, pre-eclampsia, multi-pregnancy → ↑Risk of stillbirth

Twins

- ICP + twin pregnancy → higher risk of stillbirth



Antenatal care

- Atypical presentation** → Order more investigation
- Monitoring**
 - **Maternal** → repeating **LFT & Bile acid** 1 week after diagnose then depend on individual basis
 - **Fetus** → **U/S&CTG** *doesn't prevent* stillbirth
 → Monitor **fetal movements** → report concerns
- Treatment** :
 - **Role of Tx** is to reduce maternal itching not changing the outcome or bile acid level
 - ** **Ursodeoxycholic acid (UDCA)**: preferred treatment for pruritus
 - ** **Topical emollients**: for skin relief
 - ** **Antihistaminic agent** : Chlorphenamine (Uncertain)

Mild ICP → Start **Weakly** investigation when they reach **38 W**
 Moderate ICP → Start **Weakly** investigation when they reach **35 W**
 Sever ICP → frequent routine testing *isn't always necessary* in these cases, it doesn't change clinical decisions about her care

Time of delivery



Mode of delivery : According to obstetric indication

Intrapartum Care

Continuous electronic fetal monitoring when **BA > 100** or presence of **risk factor**

No risk of PPH in **uncomplicated ICP**

Consider **stander analgesia and anesthesia** for women who have **uncomplicated ICP**

Post partum

Breastfeeding: ICP is **not a contraindication**; UDCA discontinued at labor
UDCA present in breast milk in small amount **up to 4 week** and doesn't harm neonate

follow-up: **≥4 weeks postpartum** to confirm resolution
check LFTs/bile acids; refer to hepatologist if abnormal

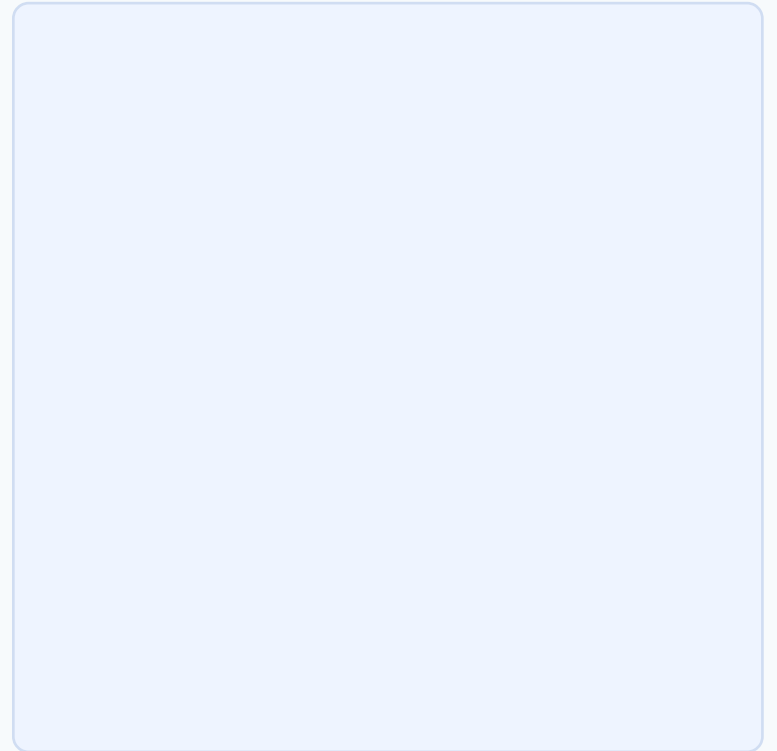
Recreant rate of ICP in next pregnancy up to **90%**
so Perform baseline LFTs and bile acids at booking

Contraceptive method

Category 1 (UKMEC): Copper IUD, levonorgestrel IUS, progestogen-only implant/injection/pill → **safe**
Compound hormonal Contraceptive → **Safe after normalization of LFTs**, with no history of contraceptive-related cholestasis

Fatty Liver of Pregnancy and Acute Cholecystitis

Presented by Nagd Mahmoud



Acute Fatty Liver of Pregnancy

- Definition and epidemiology
- Pathophysiology and risk factors
- Presentation and Swansea-based diagnosis
- Management and complications

Acute Cholecystitis in Pregnancy

- Why pregnancy predisposes to gallstones
- Symptoms and differential diagnosis
- Laboratory tests and imaging
- Medical versus surgical treatment

AFLP is a rare but life-threatening obstetric emergency that usually appears in the third trimester or early postpartum period and can rapidly progress to liver failure.

Key facts

- Rare: about 1 in 10,000-20,000 pregnancies
- Usually late pregnancy
- Symptoms may be nonspecific at first
- Can overlap with HELLP syndrome and severe preeclampsia

Why it matters

- Coagulopathy and hypoglycemia can develop quickly
- Renal dysfunction and encephalopathy may occur
- Delayed diagnosis worsens maternal and fetal outcomes

Pathophysiology

- Associated with impaired mitochondrial fatty-acid oxidation
- Classically linked to fetal fatty-acid oxidation defects such as LCHAD deficiency
- Microvesicular fat accumulates in hepatocytes and impairs liver function

Risk factors

- Primigravida
- Multiple gestation
- Male fetus
- Previous history of AFLP
- Possible fetal fatty-acid oxidation disorder

Clinical presentation

- Nausea, vomiting, malaise, abdominal pain
- Right upper quadrant or epigastric discomfort
- Jaundice may appear later
- Polydipsia/polyuria may occur
- Severe disease: confusion or bleeding tendency

Examples from the Swansea criteria: vomiting, abdominal pain, polydipsia/polyuria, encephalopathy, bilirubin elevation, hypoglycemia, leukocytosis, renal impairment, coagulopathy, and ascites or bright liver on ultrasound.

Diagnostic clues

- Abnormal AST/ALT and bilirubin
- Hypoglycemia is a major red flag
- Prolonged PT/INR and low fibrinogen suggest severe disease
- Renal impairment, leukocytosis, or ammonia elevation may coexist
- Swansea criteria support the diagnosis

Management priorities

- Urgent admission and multidisciplinary care
- Maternal stabilization with IV fluids, glucose, and blood products as needed
- Close monitoring of liver, kidney, coagulation, and mental status
- Prompt delivery once maternal stabilization has started

Complications

- Disseminated intravascular coagulation
- Acute kidney injury
- Hepatic encephalopathy
- Pancreatitis or postpartum hemorrhage
- Preterm birth, fetal distress, or fetal loss

Acute cholecystitis is inflammation of the gallbladder, usually caused by cystic duct obstruction from gallstones.

Why pregnancy increases risk

- Estrogen increases cholesterol secretion into bile
- Progesterone reduces gallbladder emptying and promotes stasis
- Biliary sludge and gallstones become more likely in pregnancy

Useful background

- Gallstone disease is common, but acute cholecystitis is much less common
- Pain location can shift as pregnancy progresses
- Symptoms may mimic other obstetric or abdominal emergencies

Clinical presentation

- Right upper quadrant pain is classic
- Pain may radiate to the shoulder, scapula, or back
- Nausea, vomiting, anorexia, and fever are common
- Murphy sign may be displaced or less obvious in pregnancy
- Tachycardia and localized tenderness may be present

Differential diagnosis

- Biliary colic
- AFLP
- HELLP syndrome
- Pancreatitis
- Peptic ulcer disease
- Lower lobe pneumonia
- Placental abruption when the presentation is atypical

Laboratory workup

- CBC for leukocytosis
- Liver tests and bilirubin to assess obstruction or cholestasis
- Consider lipase if pancreatitis is possible
- Assess hydration status and maternal-fetal well-being

Imaging approach

- Ultrasound is the first-line imaging test
- If ultrasound is nondiagnostic, MRI/MRCP is a useful radiation-free next step
- CT is usually avoided unless clearly necessary
- ERCP is reserved for suspected choledocholithiasis or cholangitis when intervention is needed

Initial treatment

- NPO or bowel rest
- IV fluids and analgesia
- Antiemetics and maternal-fetal monitoring
- Antibiotics when infection is suspected or symptoms persist
- Antibiotic choice should follow local guidance

When surgery is favored

- Failure of conservative management
- Recurrent attacks during pregnancy
- Complicated disease: gangrene, perforation, cholangitis, or pancreatitis
- Guidelines support laparoscopic cholecystectomy rather than repeated nonoperative care for acute cholecystitis during pregnancy

AFLP vs Acute Cholecystitis: Quick Comparison

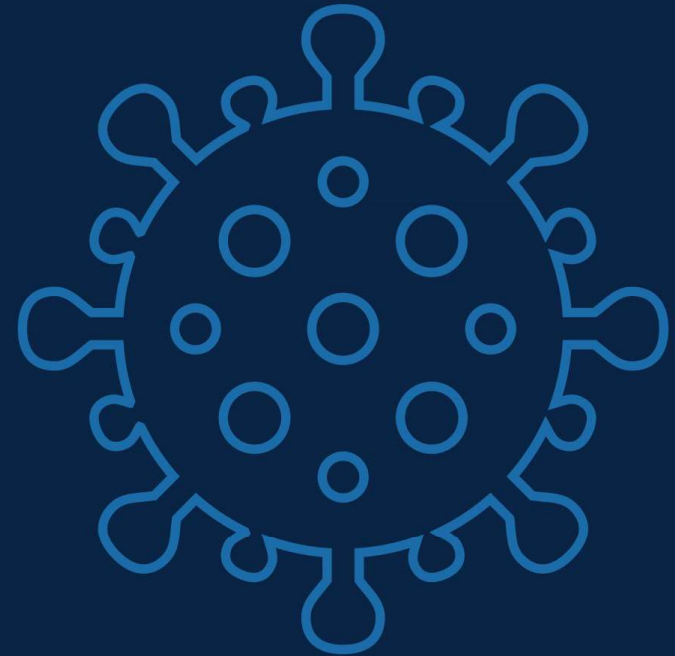
Summary

Feature	AFLP	Acute cholecystitis
Typical timing	Third trimester / early postpartum	Any trimester when gallstones become symptomatic
Main process	Pregnancy-specific liver failure syndrome	Gallbladder inflammation usually from stones
Key red flags	Hypoglycemia, coagulopathy, encephalopathy	Fever, RUQ pain, and ultrasound findings
Definitive step	Delivery	Cholecystectomy when indicated

1. AGA Clinical Practice Update on Pregnancy-Related Gastrointestinal and Liver Disease. *Gastroenterology*. 2024.
2. AASLD Practice Guidance: Reproductive Health and Liver Disease.
3. SAGES Guidelines for the Use of Laparoscopy During Pregnancy.
4. IDSA 2024 guideline update on diagnostic imaging of suspected acute cholecystitis and cholangitis in adults, children, and pregnant people.
5. Nelson DB, Byrne JJ, Cunningham FG. Acute fatty liver of pregnancy. *Obstet Gynecol*. 2021.
6. Uploaded file used as an outline and pregnancy-specific background: *Hepatic-Disorders-In-Pregnancy copy copy.pdf*.

VIRAL HEPATITIS IN PREGNANCY

Epidemiology · Clinical Features · Management · Outcomes



Sources: Williams Obstetrics · Obstetrics by Ten Teachers · Sherlock's Liver & Biliary System · Mandell's Infectious Diseases

OVERVIEW

#1

Cause of Jaundice
in Pregnancy

Hep E

Highest Mortality
Risk (20–53%)

Hep B & C

Vertical Transmission
Most Common

6%

Hepatitis Patients
Develop Cholelithiasis

Key Clinical Principles

- Acute viral hepatitis is the most common cause of jaundice in pregnancy.
- The course of most viral infections is not significantly altered by pregnancy.
- Hepatitis B and C can be transmitted to the baby at or around the time of birth (perinatal/vertical transmission).
- Hepatitis E carries the highest risk in pregnancy — 20% of those infected in the 3rd trimester develop fulminant hepatic failure.
- Most women with hepatitis will have a normal pregnancy; however, physiological changes in pregnancy can stress hepatic function.

VIRAL HEPATITIS — COMPARATIVE OVERVIEW

Virus	Nucleic Acid	Transmission	Incubation	Chronic Infection	Vaccine
Hepatitis A	ssRNA	Fecal–oral	15–50 days	No	Yes
Hepatitis B	dsDNA	Parenteral, sexual	30–180 days	>90% infants <10% adults	Yes
Hepatitis C	ssRNA	Parenteral	14–180 days	75–80%	No
Hepatitis D	Circular RNA	Parenteral, sexual (requires HBV)	42–180 days	Superinfection: 75% Coinfection: 5%	Via HBV vaccine
Hepatitis E	ssRNA	Fecal–oral	21–56 days	Rare (immunosuppressed)	Yes*

* Approved only in China | HBV = Hepatitis B Virus | HCC = Hepatocellular Carcinoma

Hepatitis A Virus (HAV)

Section 1 of 4

Virus Snapshot

Family

Picornaviridae

Genome

Single-stranded RNA, non-enveloped

Route

Fecal-oral (contaminated food/water)

Incubation

15–50 days, short viremia

Chronicity

Does NOT cause chronic infection

Vaccine

Available — inactivated virus

HEPATITIS A | Epidemiology & Clinical Features

Maternal Symptoms

- Malaise, fatigue, anorexia, nausea
- Right upper quadrant / epigastric pain
- Jaundice (may be the presenting sign)
- Upper abdominal tenderness on examination
- Hepatomegaly
- Affects ~1 in 1,000 pregnant women in the UK
- Travelers to endemic regions are highest-risk

Effects on Pregnancy

- Intra-uterine (vertical) transmission is very rare
- Perinatal transmission is possible near time of birth
- Preterm labour
- Placental abruption
- Premature rupture of membranes

Diagnosis

IgM anti-HAV (ELISA) · Elevated ALT & Bilirubin · PCR of feces · Hyperammonemia → significant liver injury

HEPATITIS A | Management

No Specific Treatment

Recovery is supportive and may take several weeks to months. The primary goal is to avoid complications.

Avoid Unnecessary Medications

Paracetamol should be avoided due to hepatotoxic risk. Unsafe anti-emetics are also contraindicated.

Vaccination — Safe in Pregnancy

Inactivated virus vaccine. Indicated if exposure risk is high. ~70% develop protective antibodies 2 weeks after dose 1. Partner should also be vaccinated.

Breastfeeding

Breastfeeding is NOT contraindicated in HAV. Mothers may continue nursing.

Hepatitis E Virus (HEV)

Section 2 of 4

30–53%

Maternal Mortality

69%

Fetal Mortality

20%

Fulminant Failure
(3rd trimester)

 **Most dangerous hepatitis in pregnancy**

HEPATITIS E | Clinical Features, Outcomes & Management

Overview & Risk

- Leading cause of acute viral hepatitis (AVH) in developing countries
- Severity varies by region: more severe in India, less so in Egypt, Europe, USA
- Pregnant women are disproportionately vulnerable to HEV vs other hepatitis viruses
- Mechanism of high morbidity in pregnancy remains incompletely understood
- Can develop into a chronic infection in immunosuppressed individuals
- Diagnosis: Anti-HEV IgM/IgG; Western blot for confirmation

Effects on Pregnancy (Vertical Transmission)

- ▶ Preterm delivery
- ▶ Miscarriage
- ▶ Stillbirth
- ▶ Neonatal death

Management

- Prevention: good sanitation and vaccination
- Treatment: mainly supportive
- Breastfeeding: UNSAFE during active symptomatic infection
- Ribavirin: contraindicated in pregnancy (teratogenic); stop 6 months before conception

Hepatitis B Virus (HBV)

Section 3 of 4



**2 billion people
infected worldwide**



**>350 million
chronic carriers**



**0.5–1% prevalence
in UK pregnant women**



**85% infant
chronic carriage
if mother is eAg+**

dsDNA virus · Parenteral, sexual, & vertical transmission

HEPATITIS B | Screening & Clinical Features

Screening — Universal Recommendation (UK National Screening Committee)

- All pregnant women should be offered serological screening for HBV at booking.
- Screening detects HBsAg carriers and enables effective postnatal prophylaxis to reduce vertical transmission.
- 85% of infants born to eAg-positive mothers will become chronic HBsAg carriers vs. 31% for eAg-negative mothers.
- Chronic HBsAg carriers are 22× more likely to die from hepatocellular carcinoma (HCC) or cirrhosis than non-carriers.

Clinical Features

- Incubation: 6 weeks – 6 months
- Many patients are completely asymptomatic
- Acute HBV course is not significantly altered by pregnancy
- Chronic active hepatitis → increased risk of prematurity, low birthweight, neonatal death

Oriental Women & HBV

Prevalence of HBsAg varies widely across ethnic groups. Women of East Asian origin have a significantly higher prevalence and should be counselled accordingly. HBV is highly endemic in parts of East Asia (e.g. China), where vertical transmission is very common.

HEPATITIS B | Management & Immunoprophylaxis

~95%

Mother-to-child transmission of HBV is approximately 95% preventable through combined administration of Hepatitis B Immunoglobulin (HBIG) + vaccine at birth.

Active Vaccine Schedule (3 doses)



Additional Management Notes

- HBIG provides immediate passive protection against virus transmitted during delivery — given immediately after birth.
- Exception: HBIG is **not required** if the mother carries anti-HBe antibodies (non-infective status) — babies of these mothers receive vaccine only.
- Combined HBIG + vaccine is superior to either alone.
- HBV-positive mothers should be referred to a hepatologist for long-term monitoring (HCC surveillance).
- Women presenting in labour without booking bloods → urgent HBsAg serology, immunize within 24 hrs if positive.

Hepatitis C Virus (HCV)

Section 4 of 4

HCV at a Glance

Genome

ssRNA (Flaviviridae)

Transmission

Blood products, IV drug use, tattooing, body piercing

Sexual Transmission

Extremely rare

Mother-to-child

~3–5% risk (rises to ~36% with HIV co-infection)

Chronicity Rate

75–80%

UK Antenatal Prev.

~1% (regional variation)

HEPATITIS C | Screening, Clinical Features & Management

Screening Policy

Routine screening for HCV is NOT recommended in pregnancy (insufficient evidence for effective interventions). Selective screening is offered for high-risk women: IV drug use, HBV/HIV co-infection. Method: Anti-HCV IgG antibodies → confirmatory PCR if positive.

Clinical Features

- 80% of initial infections are asymptomatic; only 20% present with hepatic symptoms
- Most pregnant women with HCV are unaware of their infection
- Long-term consequences: cirrhosis, HCC, liver failure
- Adverse pregnancy outcomes: preterm rupture of membranes, gestational diabetes (GDM)
- Neonatal: low birthweight, NICU admission
- Vertical transmission risk **increases with higher maternal viral load** — HCV RNA quantification should be considered in seropositive women.

Management

- Positive anti-HCV → confirmatory PCR → refer to hepatologist
- Interferon + Ribavirin: CONTRAINDICATED in pregnancy (teratogenic)
- No consensus on mode of delivery — elective C-section NOT routinely recommended
- Caesarean section IS recommended if co-infected with HIV
- Breastfeeding: generally not contraindicated unless nipples cracked/bleeding

VIRAL HEPATITIS IN PREGNANCY — MANAGEMENT SUMMARY

Feature	Hep A	Hep E	Hep B	Hep C
Specific Treatment	None (supportive)	None (supportive)	Antivirals (chronic)	Antivirals*
Vaccine Available	✓ Yes	✓ (China only)	✓ Yes	✗ No
Vertical Transmission	Rare	Yes (common)	Yes (85% if eAg+)	3–5% (36% w/ HIV)
Breastfeeding	Safe ✓	Unsafe ✗ (active)	Safe ✓	Generally safe
Maternal Mortality	Low	30–53%	Low	Low (long-term risk)
Pregnancy Screening	Not routine	Not routine	Universal ✓	High-risk only

* Interferon + Ribavirin contraindicated in pregnancy

New Developments & Future Directions

- HBV vaccination programmes have significantly reduced childhood hepatocellular carcinoma (HCC). Taiwan's national HBV immunisation programme, initiated in 1984, demonstrated a measurable decline in HCC incidence among vaccinated children — a landmark example of cancer prevention through vaccination.
- HCV in pregnancy remains an area of active research. Current antivirals (interferon + ribavirin) are contraindicated due to teratogenicity. Further studies are needed to evaluate safe and effective antiviral options for pregnant women with HCV.
- HEV vaccine (HEV 239 / Hecolin) is currently approved and in use in China. Global deployment remains limited; research into its safety profile in pregnancy and broader international licensure is ongoing.
- The role of universal antenatal HCV screening is under active debate. Current UK guidance recommends selective (high-risk) screening only, but emerging evidence supports reconsidering this approach as treatment options evolve.
- Global reduction of the hepatitis burden remains a WHO priority. Elimination targets for HBV and HCV by 2030 include improved antenatal screening, vaccination coverage, and access to treatment in low-resource settings.

References: Williams Obstetrics (Cunningham et al.) · Obstetrics by Ten Teachers · Dewhurst's Obstetrics & Gynaecology · Sherlock's Diseases of the Liver · Mandell's Principles of Infectious Diseases · Nelson Textbook of Paediatrics

Key Takeaways

- HAV & HEV are fecal–oral; supportive care only — HAV vaccine is safe in pregnancy.
- HEV carries the highest maternal and fetal mortality — screen in endemic regions.
- HBV: universal antenatal screening + HBIg + vaccine at birth prevents ~95% of vertical transmission.
- HCV: selective screening for high-risk groups; antiviral therapy is contraindicated in pregnancy.
- All hepatitis types require multidisciplinary care (obstetrics + hepatology).

References: Williams Obstetrics (Cunningham et al.) · Obstetrics by Ten Teachers · Dewhurst's Obstetrics & Gynaecology · Sherlock's Diseases of the Liver · Mandell's Principles of Infectious Diseases · Nelson Textbook of Paediatrics