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Acute Viral Hepatitis

★ Objectives:

1. Recognise the different type of acute viral hepatitis
2. Know the possible complications and outcome of acute viral hepatitis
3. Aware of the other cause of acute hepatitis in KSA
4. To have fair knowledge about the latest results of epidemiological aspect of viral hepatitis A,B,C IN KSA

★ **Resources Used in This lecture:** Master the boards, Kumar, Pathoma, Lecture slides.

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Hepatitis

Definition:

Hepatitis is an inflammation of the liver.

Causes

Infectious

- HAV , HBV , HCV , HDV , HEV (5 main categories of viral hepatitis A,B,C,D,E.)
- Other include :EBV,CMV and HSV seen in immunocompromised patients

Classified into:

- Acute viral hepatitis. : last less than 6 Months
- Chronic viral hepatitis. : last More than 6 Months

Non-infectious

- Alcohol
- Drug-induce
- Autoimmune disorder (More common in young women with a positive **ANA/ANF(antinuclear antibody/factor such as** liver-kidney microsomal antibodies. , High gamma globulin (IgG). ,Anti-smooth muscle antibodies. The most accurate test is the liver biopsy. Treat with prednisone and or azathioprine.
- Hereditary diseases

Root of transmission:

- A & E from food and water. (fecal-oral route)
- B,C,D from Sex,blood, parenteral.

- HDV is unable to replicate on it's own , it needs a person with active viral replication of hepatitis B.
- HEV in pregnant women is associated with fulminant hepatitis. (worst in pregnancy)
- HEV is prevalent in developing countries such as India , Pakistan and parts of Africa.
- Mnemonic⟶ You **A**te hepatitis **A**; you **E**at hepatitis **E**.

Acute Viral Hepatitis

Presentation.

- Jaundice.
- Right upper quadrant abdominal pain.
- Fever, weight loss, and fatigue.
- Dark urine. (due to high direct bilirubin)
- Hepatosplenomegaly.
- Nausea, vomiting, abdominal pain.

- No way to detect the etiology of hepatitis from the acute symptoms, because they all have same presentation.
- Most cases of acute hepatitis are from viral hepatitis **A or B.**
- Hepatitis C, rarely presents with an acute infection, and is found as a "silent" infection on blood tests or patients presenting with cirrhosis.

Phases of presentation:

There are 3 phases of Hepatitis: Pre-icteric, Icteric and Posticteric. "Icterus means jaundice."

Pre-icteric phase	Icteric phase "Jaundice"	Post-icteric phase
1. Anorexia 2. Fatigue 3. Nausea 4. Vomiting 5. Arthralgia 6. Myalgia 7. Headache 8. Photophobia 9. Pharyngitis	1. Enlarged liver 2. Tender upper quadrant 3. Discomfort 4. Splenomegaly (10-20%) 5. General adenopathy	Cessation of the symptoms, liver enlargement and continued fatigue.

Diagnostic Tests.

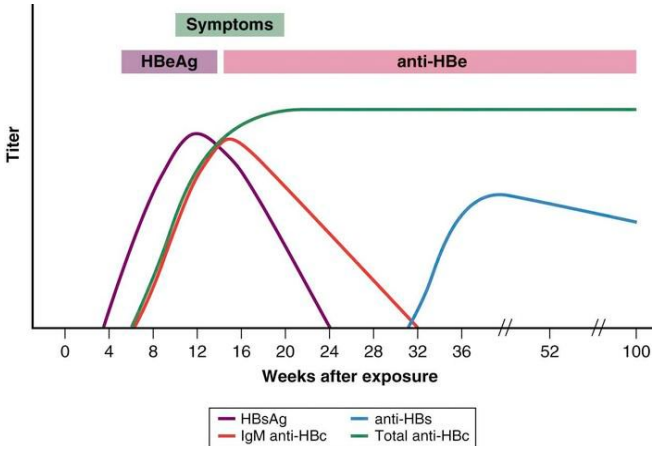
Laboratory Test

- ❏ Increased direct bilirubin.
- ❏ Liver function test (LFT) increase 5-10 times above normal, both ALT or AST (ALT Higher)
- Increased ratio of alanine aminotransferase (ALT) to aspartate aminotransferase (AST).
- ❏ Increased alkaline phosphatase

Note: Severity of Disease is assessed by the prothrombin time (PTT), and serum bilirubin.

Specific Diagnostic Tests.

- ❏ **PCR :** which tells the amount of active viral replication. (Disease activity of hepatitis)
- ❏ **Serology (antibody and antigen)**
- Hepatitis A, C, D, and E : The "best initial diagnostic test" for each of these is simply an IgM antibody for the acute infection and IgG antibody to detect resolution of infection.



- **Hepatitis B**

Serologic Patterns						
	Surface antigen (HBsAg)	Surface antibody (anti-HBs)	Core antibody (anti-HBc)	E-antigen	anti-HBe	HBV-DNA
What does it indicate?	infection (carrier)	immunity	exposure to infection	viral replication	Sero-conversion	viral replication
Acute infection	+	−	+ IgM	+		
Chronic infection	+	−	+ lgG − IgM	−		
Resolved, old, past infection (Natural infection Immunity)	−	+	+ lgG − IgM	−		
Vaccination	−	+	−	−		
"Window period"	−	−	+ lgM, and then lgG	−		
Susceptible to infection	−	−	−	−		

- Surface antigen is the only way to know the viral is present or **not**!
- If surface antigen < 6 months ⟶ acute hepatitis If >6 months ⟶ chronic Hepatitis.
- E-antigen and DNA polymerase show viral replication and shows the ability of **transmission** of the virus.

Complications.

Chronic hepatitis	Fulminant hepatitis	Aplastic anemia
Can progress to cirrhosis of HCC.	• Hepatic Failure Within 8 Weeks Of Onset Of Illness. • Manifestation: Encephalopathy and Prolonged PT • Histopathology: Massive Hepatic Necrosis.	It is a rare complication of acute hepatitis.

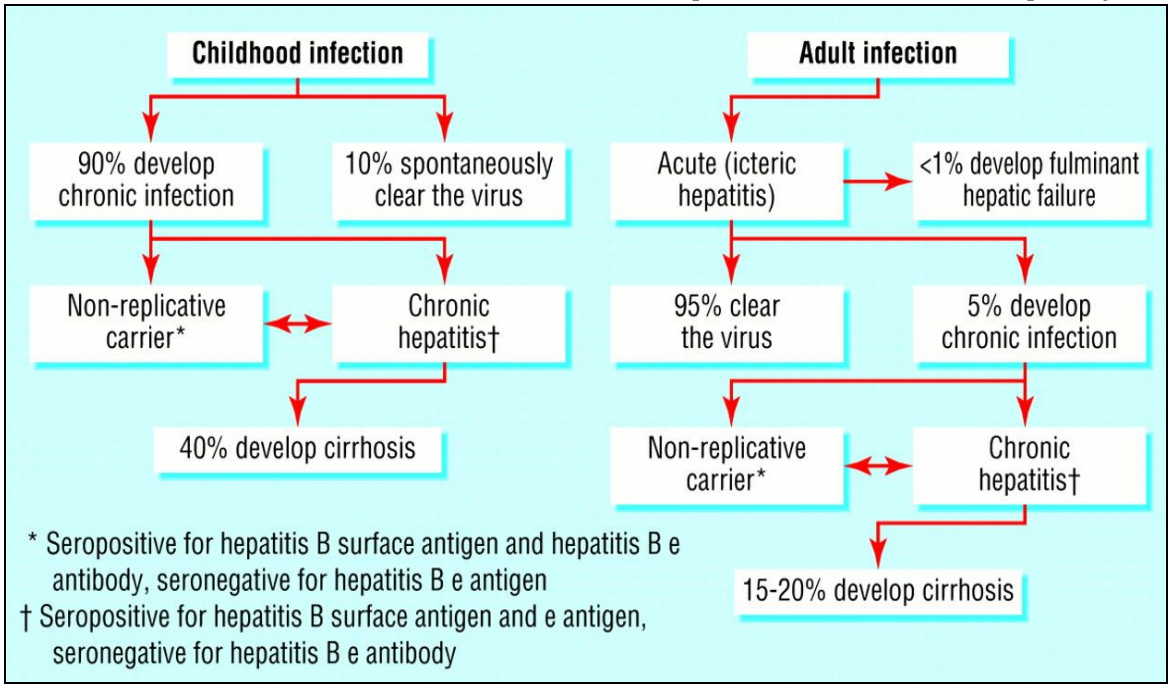
Treatment.

- Hepatitis A and E resolve spontaneously over a few weeks and are almost always benign conditions.
- Hepatitis B only treated chronically with interferon **or** lamivudine.
- Acute hepatitis C, in the few cases in which it is detected, should be treated with Interferon **and** ribavirin **and** either boceprevir or telaprevir.
- Chronic HCV Interferon **and** ribavirin or direct acting anti virus which depends of specific HCV genotype: genotype 1 → ledipasvir and sofosbuvir orally for 12 weeks, other genotypes include → sofosbuvir and ribavirin orally.

- Acute hepatitis is usually self-limiting that return to normal structure and function.
- HBV drugs act mainly on DNA polymerase that's why it needs to be chronic to be given.
- Only acute hepatitis C is **the only** form of acute hepatitis to be treated!
- Ribavirin causes anemia.
- Interferon causes flu like illness,depression, arthralgia, leukopenia and thrombocytopenia.

Prognosis.

Infections occurring in childhood, are more likely to progress into chronic infections. Whilst in adulthood, 95% of acute viral hepatitis will be cured completely.



Differential diagnosis of acute viral hepatitis.

- Infectious Mononucleosis: infection usually caused by the Epstein-Barr virus. The virus spreads through saliva. Symptoms include: Fever, sore throat and swollen lymph glands.
- Drug Induced Hepatitis: especially acetaminophen.

- Chronic Hepatitis.
- Alcohol Hepatitis
- **Cholecystitis, Cholelithiasis.**
- Autoimmune hepatitis.

PREVENTION STRATEGIES OF MINISTRY OF HEALTH IN KSA.

- Mandatory screening of blood donors and expatriates.
- Vaccination of risk groups (HBV for health workers HAV travellers mainly)
- Health education especially among medical personnel.
- Hygiene and sanitation to prevent HAV.

Summary

Virus		A	B	C	D	E
Epidemiology		Young	Any age	Any age	I.V. drug users	Any age
Spread	Faeco-oral	✓	✗	✗	✗	✓
	Blood	Rare	✓	✓	✓	✗
	Vertical	✗	✓ (B = Baby)	Rare	Occasional	✗
	Saliva	✓	✓	✓	✗	?
	Sexual	Rare	✓	Rare	Rare	✗
Carrier state		✗	✓	✓	?	✗
Chronic liver disease		✗	✓	✓	✓	✗
Liver cancer		✗	✓	Rare	✓	✗
Vaccine		✓	✓	✗	✗	✗
Prevention		pre/post-exposure immunization	pre/post-exposure immunization	Blood donor screening; risk behaviour modification	pre/post-exposure immunization; risk behaviour modification	Ensure safe drinking water
Diagnosis		• IgM anti-HAV in serum → active infection. • IgG anti-HAV in serum → indicates past infection	Please check the table below.	• HCV-RNA: confirms infection • Decreased RNA: recovery. • persistence RNA: chronic.	• HDV-RNA in serum. • IgM anti-HDV in serum	• HEV igM • HEV igG • HEV RNA PCR

	(immunization)		● ANTI -HCV		

MCQ's.

1.Which of the following correlates the best with an increased likelihood of mortality?
a. Bilirubin
b. Prothrombin time
c. ALT
d. AST
e. Alkaline phosphatase

Answer: B. All of these lab tests can be markedly elevated during acute hepatitis with little adverse significance except for prothrombin time (PT). If the PT is elevated, there is a markedly increased risk of fulminant hepatic failure and death.

2. Which of the following will become abnormal first after acquiring hepatitis B infection?
a. Bilirubin
b. e-antigen
c. Surface antigen
d. Core lgM antibody
e. ALT
f. Anti-hepatitis B e-antibody

Answer: C. Surface antigen is a measure of actual viral particles. Bilirubin, ALT, and antibody production are a measure of the body's response to the infection.

3.Which of the following is the most direct correlate with the amount, or quantity, of active viral replication?
a. Bilirubin
b. e-antigen
c. Surface antigen
d. Core lgM antibody
e. ALT
f. Anti-hepatitis 8 e-antibody

Answer: B. Although surface antigen is a measure of whether there is any viral replication or infection at all, surface antigen does not tell quantity. Hepatitis B e-antigen is directly correlated with the degree of DNA polymerase. E-antigen is present only when there is a high level of DNA polymerase activity.

4.Which of the following indicates that a patient is no longer a risk for transmitting infection to another person (active infection has resolved)?
a. Bilirubin normalizes
b. No e-antigen found
c. No surface antigen found
d. No core lgM antibody found
e. ALT normalizes
f. Anti-hepatitis 8 e-antibody

Answer: C. As long as surface antigen is present, there is still some viral replication potentially occurring. Even if surface antibody were one of the choices, the correct answer would still be surface antigen. Transmissibility ceases when DNA polymerase ceases, not when surface antibody appears. jaundice (increased bilirubin) and elevated
ALT will all normalize long before viral replication stops. You can definitely have viral replication, elevated DNA polymerase, and positive surface antigen with a normal ALT.Hepatitis B e-antibody will appear prior to resolution of all DNA polymerase activity. It is an indication that the acute infection is moving toward resolution, but it does not conclusively prove resolution has occurred.

5.Which of the following is the best indication of the need for treatment with antiviral medications in chronic disease?

a. Bilirubin
b. e-antigen
c. Surface antigen
d. Core lgM antibody
e. ALT
f. Anti-hepatitis B e -antibody

Answer: B. The person most likely to benefit from antiviral medications is the one with the greatest degree of active viral replication. Hepatitis B e-antigen is the strongest indicator of active viral replication. Although surface antigen means there is at least some active disease, it might be on the way to spontaneous resolution and would not benefit. Everyone with e-antigen also has surface antigen. The person with the worst disease (highest DNA polymerase) will benefit the most from treatment.

6. Which of the following is the best indicator that a pregnant woman will transmit infection to her child?

a. Bilirubin
b. e -antigen
c. Surface antigen
d. Core lgM antibody
e. ALT
f. Anti-hepatitis B, e-antibody

Answer: The correct answer is e-antigen. Your questions may offer DNA polymerase as a choice instead of e-antigen. Any time you would say e-antigen, you would also say DNA polymerase. The only difference is that e-antigen is a qualitative test, meaning it is simply positive or negative. DNA polymerase is a quantitative test, meaning you get a level that can have a lot of variability. It is like the gas tank in your car. Hepatitis B e-antigen tells you, "Gas present: yes or no." DNA polymerase is like the gauge on your tank: It tells an amount. If a woman is positive for surface antigen, but thee-antigen is negative, only 10% of children will become infected with hepatitis B at birth. When both surface antigen and e-antigen are positive, 90% of children will be infected at birth. This is why perinatal transmission is the most common method of transmission worldwide.

Thank you..