

## LFTs Seminar Notes

- LFTs include albumin, glucose, bilirubin (total and direct), AST, ALT, alkaline phosphatase, PT and PTT. They provide information about the liver's:
  - a- **Synthetic function**: glucose, albumin, protein and INR
  - b- **Bile conjugation and excretion**: bilirubin
  - c- **Injury and inflammation**: ALT and AST
  - d- **Storage**: glucose, TGs, Vitamins (ADEK), copper
- **ALT is more specific to liver injury**; since AST can be elevated due to injuries of other tissues other than the liver, such as the cardiac muscle (MI), kidneys, skeletal muscles (rhabdomyolysis), brain, and red blood cells (hemolysis).
- **Alkaline phosphatase** is mostly found in the biliary endothelium (cholestatic diseases), bones (metastases), placenta (pregnancy), and intestine (infarction).
- To confirm that alk phosphatase is elevated in biliary damage due to a cholestatic cause, **GGT** is checked (should be elevated).
- **Acute liver failure** is the rapid deterioration of liver function in a patient not known to have a chronic liver disease (e.g. cirrhosis) associated with mental status changes (hepatic encephalopathy) and elevated INR.
- **Acute liver injury** is the elevation in liver enzymes without being associated with hepatic encephalopathy and elevated INR.
- **Liver injury patterns** can be hepatocellular, cholestatic, or mixed. Each caused by different types of diseases.

Pattern	ALT	AST	ALP	GGT	Bilirubin
<b>Hepato-cellular</b>	↑↑	↑↑	±↑	±↑	±↑
• Viral	Often AST<ALT		±↑	±↑	±↑
• NAFLD			±↑	±↑	±↑
• Alcoholic	AST:ALT ≥ 2:1		±↑	↑	±↑
• Ischemic <small>shock; liver shutting down</small>	↑↑↑	↑↑↑	↑↑	±↑	↑↑
<b>Cholestatic</b>	+/-↑	+/-↑	↑↑	↑↑	↑↑
<b>Mixed</b>	<b>R ratio = (ALT/ALT ULN) / (ALP/ALP ULN)</b> > 5 = hepatocellular; < 2 = cholestatic; 2 – 5 = mixed				

## Cases

### Normal ranges:

- **ALT.** 7 - 55 U/L
- **AST.** 8 - 48 U/L.
- **ALP.** 40 - 129 U/L.
- **Albumin.** 3.5 - 5.0 g/dL
- **Total protein.** 6.3 - 7.9 g/dL.
- **Bilirubin.** 0.1 - 1.2 mg/dL
- **GGT.** 8 - 61 U/L.
- **LD.** 122 - 222 U/L.

1- A 21 yr old female presents with mild RUQ pain, nausea and vomiting.  
Labs show:

- ALT 7,000 IU/L
- AST 5,800 IU/L
- Total bilirubin 3 mg/dL
- Alkaline phosphatase 85 IU/L
- INR 2.5
- serum pH 7.28

- ⇒ **Pattern of abnormality:** hepatocellular, since ALT & AST are mainly elevated.
- ⇒ **Cause:** pt is young with mild symptoms, there is acidosis which suggests a drug-induced liver injury secondary to acetaminophen for example. It is the most common cause of liver injury in young patients.
- ⇒ Antidote to acetaminophen toxicity of <4hrs is activated charcoal, if >4hrs, Acetylcysteine.

2- 70 yr old female with DM-2, hypertension admitted to the ICU with severe pneumonia. Labs show:

- ALT 1,900 IU/L
- AST 2,500 IU/L
- LDH 2,200 U/L

- ⇒ **Pattern of abnormality:** hepatocellular
- ⇒ **Cause:** ischemic hepatitis secondary to sepsis; since AST>ALT and LDH is elevated which usually indicates tissue damage (due to infection for example).
- ⇒ If the ALT:LDH ratio is <1.5 we suspect ischemic hepatitis.

3- 45 yr old male referred from prison because of malaise and nausea.

Labs show:

- ALT 2100 IU/L
- AST 1300 IU/L
- LDH 350 U/L

⇒ **Pattern of abnormality:** hepatocellular

⇒ **Cause:** viral hepatitis; we can see prodrome symptoms, enzymes are in the thousands, and LDH is elevated. Probably HBV; since the patient is 45Y and high-risk behaviors associated with being in prison (drug use).

⇒ If the ALT:LDH ratio is  $>4.5$  we suspect acute viral hepatitis.

▪ **In Summary:**

When ALT and AST enzymes are in the thousands, we think of 3 main causes: drug-induced, acute hepatitis and ischemic hepatitis. Other less common causes are autoimmune hepatitis, acute Wilson's disease and acute common bile duct obstruction. Diagnosing depends on the presentation of the patient.

Case 1 is a young female patient with no mentioned comorbidities or high risk behaviors. The most common cause of acute liver injury/failure in this age group is DILI due to acetaminophen (especially that serum pH was provided in the question stem which we usually check in DILI and has a poor prognostic indication in cases of acetaminophen toxicity if pH is  $< 7.3$ ).

Case 2 is an old patient with multiple comorbidities who appears to be sick and most likely hypotensive in the ICU. The key is noting the very elevated LDH (ALT to LDH ratio  $< 1.5$ ) which is most consistent with ischemic hepatitis.

Case 3 A patient from prison with likely high risk behaviors (IVDU, common to get tattoos in prison etc). The key also to differentiate from other causes of severely elevated liver enzymes is the ALT to LDH ratio  $> 4.5$  which is very suggestive of acute viral hepatitis most likely hepatitis B. If you answered Hep A could be correct (but less likely given his age).

4- A 42 yr old female with history of Graves' disease presents with one month history of fatigue. Labs show:

- ALT 570 IU/L
- AST 420 IU/L
- Alk phos 80 IU/L
- Total bilirubin 1.0 mg/dL

⇒ **Pattern of abnormality:** hepatocellular

⇒ **Cause:** autoimmune type 1 hepatitis (AIH-1); pt is an old female.

⇒ **Investigations:** ANA, anti-SMA Ab, gamma globulin (serum IgG). If the patient was younger (AIH-2), we check LKM1 Ab.

⇒ AI conditions associated with AIH are graves', diabetes, IBD, vitiligo, lupus, and RA.

5- A 42 yr old female with hx of scleroderma presents with 2 month history of fatigue and pruritus. Labs show:

- ALT 40 IU/L
- AST 35 IU/L
- Alk phos 390 IU/L
- Total bilirubin 1.2 mg/dL

⇒ **Pattern of abnormality:** cholestatic; alk phosphatase is mainly elevated >2x.

⇒ **Cause:** primary biliary cholangitis, which is associated with scleroderma and occurs more in females in their early 40s

⇒ PBC is associated with scleroderma, Sjogren's syndromes, autoimmune thyroiditis.

⇒ **Investigation:** AMA

6- A 55 yr old male with DM-2, hypertension and obstructive sleep apnea found to have hepatomegaly upon routine exam. Labs show:

- ALT 100 IU/L
- AST 60 IU/L
- Alk phos 80 IU/L
- Total bili 0.9 mg/dL

⇒ **Pattern of abnormality:** hepatocellular

⇒ **Cause:** NAFLD (ALT>AST). Patient is middle-aged with metabolic syndromes risk factors and OSA which is associated with NAFLD. He also has hepatomegaly.

**7-** 29 yr old male presents to the ED with altered mental status. Labs show:

- ALT 120 IU/L
- AST 320 IU/L
- Alk phos 130 IU/L
- Total bilirubin 10 mg/dL
- INR 2.2

⇒ **Pattern of abnormality:** hepatocellular

⇒ **Cause:** alcoholic hepatitis (AST : ALT >2, but don't exceed 400). Total bilirubin is characteristically high in severe alcoholic hepatitis and change in mental status with prolonged INR could be due to acute liver failure secondary to acute alcoholic hepatitis.

⇒ Altered mental status could be due to delirium due to alcohol or hepatic encephalopathy which could happen with severe alcoholic hepatitis even without cirrhosis.

**8-** 20 yr old female presents with jaundice. Labs show:

- ALT 800 IU/L
- AST 1,200 IU/L
- Alk phos 20 IU/L
- Bili 25 mg/dL
- INR 3
- Hgb 9 g/dL
- Cr 2 mg/dL

⇒ **Pattern of abnormality:** hepatocellular

⇒ **Cause:** Wilson's disease. Patient is young presenting with jaundice and AST>ALT (each exceeding 400) while alk phosphatase is below normal (characteristic of acute Wilson's disease). She is also coagulopathic with hemolytic anemia and acute kidney injury.

⇒ Alk phos : Total bilirubin ratio of <2 is seen in Wilson's disease.