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Gastroenterology & Hepatology
Advanced Practice Providers

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Elevated Liver Enzymes

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Disclosures

Amanda Chaney, DNP, APRN, FAANP, AF-AASLD

Speakers Bureau: Mallinckrodt, Clinical Area – Hepatorenal Syndrome

Advisory Board: Salix, Clinical Area – Hepatic Encephalopathy

Author: Springer Publishing, Clinical Area – GI & Liver Disease

The Liver's Functions

Synthesis of:

- Albumin
- Clotting factors
- Fibrinogen
- Prothrombin

Metabolism of:

- Amino acids
- Cholesterol
- Fat
- Glucose

Detoxification of substances

- Medications
- Ammonia (NH_3 ➡ urea)

Immune system activation and tolerance (Kupffer Cells)

Digestion

- Creation of bile (~ 1liter/day)
- Bile salts critical for fat soluble vitamin absorption
- Fat/Cholesterol absorption

Adapted from Barrett. 2019.

Liver ~~Function~~ Tests – Liver Biochemical Tests

Alkaline Phosphatase (Alk Phos)

Alanine aminotransferase (ALT or SGPT)

Aspartate aminotransferase (AST or SGOT)

Bilirubins (Total and Direct)

Protime/INR

Gamma-glutamyl transpeptidase (GGT)

5’-nucleotidase

Lactate dehydrogenase (LDH)

Liver Injury Tests – Cholestatic Testing

- Alkaline Phosphatase (Alk Phos or ALP) – 30-115 unit/L
- If isolated alk phos,
  - Gamma-glutamyl transpeptidase (GGT) (10-50 units/L)
  - 5’-nucleotidase
  - If above normal, then fractionation of ALP

Adapted from Kwo, et al. 2017; and AASLD. *Liver Learning*. 2016.

Liver Biochemical Tests

- Total bilirubin (0-1.0 mg/dL) and direct bilirubin (0-0.4 mg/dL)
- Albumin (3.3 – 5.0 g/dL)
  - Protein synthesized by liver
  - Low levels sign of cancer, cirrhosis or malnutrition
- INR (< 1.0)
  - Elevation reflective of poor liver function
  - Could be sign of vitamin K deficiency (malnutrition, prolonged jaundice)

Interpretation of Liver Injury

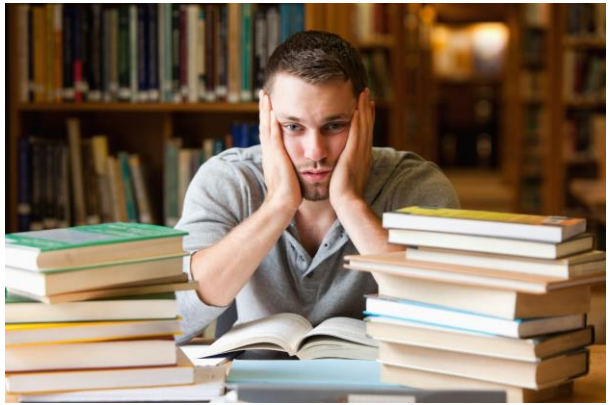
Normal levels are not concrete

Some patients with liver injury may have normal labs

Some patients with normal labs may have liver injury

Look at risk factors

Look at the patient



Abnormal Liver Testing

- Can have mixed picture
- Frequently asymptomatic
- Determine
  - **Acute** (>1 month, but <6 months)
  - **Chronic** (>6 months)
- > 10 times normal = hepatocellular/cholestatic disease
- > 25 times normal = primary hepatocellular disease

Adapted from Kwo et al. 2017; and AASLD. *Liver Learning*. 2016.

Case Study

- Mrs. S is a pleasant 55 year old female who arrives to the emergency room for a 1 week history of itching and yellowing of her skin.
- She had been diagnosed by her PCP with chronic bronchitis 2 weeks prior and was started on sulfamethoxazole- trimethoprim DS BID for 14 days, completed 7 days.
- She reports fatigue, nausea and right upper quadrant abdominal pain.

Case Study

Physical Exam:

- VS: BP 120/75, HR 90, RR 24, Temp 38.2
- Appears jaundiced with scleral icterus
- C/o severe itching
- Mild maculopapular rash to chest and back, started day of admission

Case Study

Denies history of liver disease or alcohol use

Other PMH: obesity, diabetes on metformin, hypothyroidism on Synthroid daily, chronic bronchitis

Audience Response

- Presenting Symptoms
- Which tests/labs should be offered?

Case Study

Labs from ER

- Total bilirubin 12
- Alk phos 250
- ALT 75 AST 42
- INR 1.2
- CBC – normal
- Renal profile – normal

Which Radiologic Imaging Should You Order?

A. MRI
B. CT abd w/ contrast
C. Ultrasound
D. Chest X-Ray

Steps for Evaluation

- History and Physical Exam
- Differential diagnosis based on laboratory and imaging studies
- Determine degree liver function
  - Acute liver failure
  - Chronic liver failure (cirrhosis)
    - W/ or w/o decompensation
- Complications of liver disease

What Would You Do Next?

A. Admit to hospital
B. Repeat liver panel
C. Send blood cultures and lactic acid
D. Send viral hepatitis studies
E. All of the above

Reasons for Abnormal Liver Testing

- Disease
- Infection
- Drugs
- Pregnancy

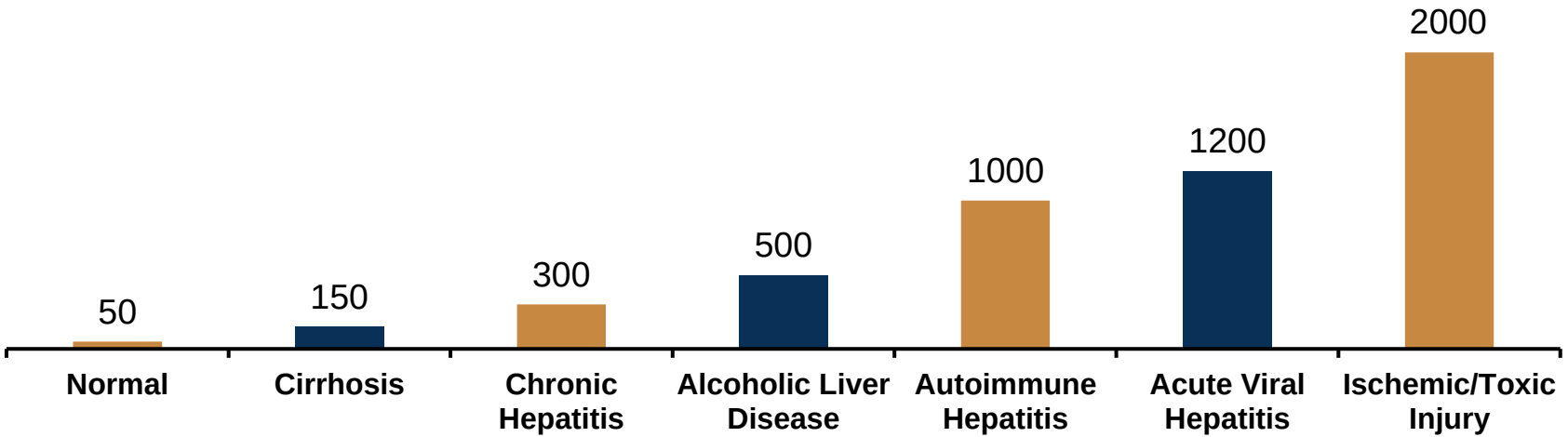
Abnormal Liver Testing

Test		Hepatocellular Injury	Cholestasis
Liver Injury Tests	**Aminotransferases** (ALT, AST)	↑↑-↑↑↑	**0**-↑
	Alkaline phosphatase	**0**-↑	↑↑-↑↑↑
Liver Function Tests	**Total/direct bilirubin**	**0**-↑↑↑	**0**-↑↑↑
	Prothrombin time (INR)	**Prolonged** (does not correct with vitamin K)	**Prolonged** (correct with vitamin K)
	Albumin	↓-↓↓↓ (chronic disease)	**0**

Abnormal ~~LFTs~~ – Abnormal Liver Testing

- Mild – moderate AST/ALT elevations in Hepatitis B or C, fatty liver, alcoholic disease
- **High elevations** of AST/ALT in toxic hepatitis, acute Hepatitis A/B or ischemic/shock liver
- Elevated bilirubin = jaundice = itching
  - Frequently with elevation in alk phos
  - Viral hepatitis
  - Drugs/alcohol/herbal
  - Biliary disease (Primary sclerosing cholangitis or Primary biliary cholangitis)

Higher ALT/AST Elevations by Diagnosis



Adapted from Giannini, 2005.

Evaluation

- ***History***
  - Alcohol consumption
  - Risk for viral hepatitis
- ***Medications***
  - Prescription
  - Over the counter
  - Herbal
  - New
  - Supplements
  - Illicit drugs
- ***Physical Exam***
- ***Risk Factors***
- ***Comorbidities***
  - Right sided heart failure
  - Diabetes/obesity
  - Inflammatory bowel disease
  - Emphysema
  - Celiac and thyroid disease

Case Study

Why does Mrs. S have hyperbilirubinemia?

A. Viral hepatitis
B. Drug reaction from sulfamethoxazole – trimethoprim
C. Fatty liver disease
D. Cholestatic disease

Drug-Induced Liver Injury (DILI)

Evaluation

Stop hepatotoxic medications

Consider drug-to-drug interactions

Additional labs

Radiologic imaging (US)

Diagnosis

- What management options are available for this patient?

Review

JHEP|Reports

Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper

Boettler T, Newsome PN, Mondelli MU, et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID *JHEP Rep*. 2020;2(3):100113. doi:10.1016/j.jhepr.2020.100113.

Tobias Boettler[1], Philip N. Newsome[2,3], Mario U. Mondelli[4], Mojca Maticic[5,6], Elisa Cordero[7], Markus Cornberg[8-9], Thomas Berg[10*].

The Usual Presentation

- Asymptomatic individual w/ mild elevation
- Differential:
  - Alcohol
  - Non-alcoholic fatty liver disease (NAFLD)
  - Medication related
- Alcohol
  - AST>ALT 2:1, ↑GGT
  - AST usually <300 IU/dL

Recommendations

- No hepatic decompensation, asymptomatic, no significant lab findings
  - Lifestyle modifications
    - No alcohol consumption
    - Weight loss
    - Controlled diabetes
  - Repeat testing in 6 months
  - If abnormal again, consider ultrasound, further labs and expert consultation

Recommendations

- If positive Hepatitis A IgM → monitor
- If positive Hepatitis B or C → monitor
  - Improved after 6 months, observe
  - Abnormal after 6 months, liver biopsy and consider expert consultation
- Abnormal iron studies
  - Stop iron supplements and alcohol consumption
  - Consider hemochromatosis testing
  - Consider liver biopsy if ongoing abnormalities

Recommendations

- Elevated alkaline phosphatase only
  - History and Physical Exam
  - GGT testing
    - Normal – etiology not hepatobiliary
    - Abnormal – Ultrasound and AMA
  - Liver biopsy if ongoing abnormalities
- AST only
  - Muscle injury?

Recommendations
(For Biliary Ductal Changes)

- Ultrasound +
  - Endoscopic retrograde cholangiopancreatography (ERCP)
  - Magnetic resonance cholangiopancreatography (MRCP)
  - AMA testing

Recommendations

- Abnormal bilirubin levels
  - Unconjugated bilirubin
    - Hemolysis testing
    - Review medications
  - Conjugated bilirubin with other LFT abnormalities
    - Ultrasound
    - ERCP/MRCP
    - Liver Biopsy

Treatment Options

- Risk for complications
- Follow Up
  - Repeat Labs
  - RTV
  - Transplant evaluation

Most Common Causes of Liver Injury

	Acute	Chronic
Hepatocellular Injury	Viral Hepatitis Drug/Toxin	Steatohepatitis (ETOH or NASH) Viral Hepatitis
Cholestatic Injury	Drug Induced Bile Duct Obstruction	Drug Induced Primary biliary cholangitis (previously known as primary biliary cirrhosis)
Questions to ask	Evidence of liver failure (H) or cholangitis (C)?	Evidence of cirrhosis?

Expert Consultation

- Unexplained, persistent elevated LFTs
- Imaging studies
- Liver biopsy
  - Performed by highly trained expert
  - Performed in a healthcare setting that is familiar with complications and their management

Liver Injury in a COVID World

- ALT/AST elevation
  - Use of lopinavir–ritonavir, with or without ribavirin, interferon beta and/or corticosteroids
  - Older age, male gender, diabetes mellitus and hypertension
- Underlying chronic liver disease in 2-11% of COVID-19 positive patients
- Many patients (14-53%) with COVID-19 developed hepatic dysfunction
- Mortality was 0-2% in patients with chronic liver disease

Adapted from Yip, Lui, Wong, et al. 2020; and Jothimani, Venugopal, Forhad, et al. 2020.

Patient Follow-Up

- Patient Care
  - Short-term Plan
    1.
    2.
    3.
  - Long-term Plan
    1.
    2.
    3.

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Q&A