

Interpretation of Abnormal Liver Function Tests

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KEYWORDS

• Liver function tests • Aminotransferases • Alkaline phosphatase • Bilirubin

HOSPITAL MEDICINE CLINICS CHECKLIST

1. In the setting of abnormal liver function tests (LFTs), review history for liver disease risk factors (alcoholism, blood transfusion, intravenous drug use, current hepatotoxic medications, or family history of liver disease).
2. In patients with liver injury, review risk factors and history along with pattern of LFTs to narrow your differential.
3. For patients with abnormal LFTs, recheck alanine transaminase, aspartate transaminase, alkaline phosphatase, bilirubin, and albumin levels in 1 to 3 months.
4. Also screen for treatable causes of hepatitis if abnormal LFTs persist for more than 6 months: hemochromatosis; autoimmune hepatitis; α_1 -antitrypsin deficiency; hepatitis B, C, and D; nonalcoholic fatty liver disease; and Wilson disease.
5. Check γ -glutamyl transferase level in patients with increased alkaline phosphatase levels to confirm hepatic origin of the enzyme.
6. If total bilirubin levels are increased, direct and indirect bilirubin fractions should be obtained. If indirect fraction is greater than 80% of total, then order a reticulocyte count and peripheral smear to exclude hemolysis.
7. Consider liver biopsy for any patient with abnormal LFTs of more than 6 months duration.

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DEFINITIONS

1. What are the different types of LFTs?

Abnormal LFTs are defined as increased levels of static biochemical tests, which include liver tests measured in serum (aspartate transaminase [AST], alanine transaminase [ALT], alkaline phosphatase [ALP], bilirubin) and measurements of biosynthetic liver function (international normalized ratio [INR], albumin).^{1,2}

2. What are normal values for LFTs?

ALT: 0 to 45 IU/L

AST: 0 to 45 IU/L

ALP: 30 to 120 IU/L

Bilirubin: 0.5 to 1.0 mg/dL

INR: 10.9 to 12.5 seconds

Albumin: 4 to 6 g/dL

3. How are normal LFTs defined?

Normal LFTs are defined as the mean distribution \pm 2 standard deviations in a representative healthy population. Therefore, statistically, 5% of all healthy individuals have abnormal liver function studies, many of which may be of no clinical significance. The interpretation of all abnormal liver chemistries must be considered in the clinical context of a given patient.

4. What are the different types of liver injury?

- Hepatocellular injury: cellular injury in the liver, causing release and increase of AST and ALT levels out of proportion to increase in ALP levels.
- Cholestatic injury: stasis of bile flow from liver to the duodenum, causing increase in the ALP level out of proportion to increase in transaminase levels.
- Mixed: increase of AST/ALT and ALP levels are not mutually exclusive, and mixed-type injuries are often found. Also, bilirubin levels can be increased in either hepatocellular or cholestatic injury.

5. What is the significance of increase of the different types of LFTs?

Increased Aminotransferase (ALT/AST) Levels

Aminotransferases participate in gluconeogenesis by catalyzing the transfer of amino groups from aspartic acid or alanine to ketoglutaric acid to produce oxaloacetic acid and pyruvic acid. ALT is found in its highest concentrations in the liver and is more specific to the liver than is AST, which is found in the liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leukocytes, and red cells. Increased AST levels are therefore less sensitive and specific for liver injury.³⁻⁵

Increased ALP Levels

ALP is associated with cellular membranes, and increased levels may be caused by injury to the liver, bone, kidneys, intestines, placenta, or leukocytes. In the liver, the enzyme is located in the bile canaliculi. Biliary obstruction increases synthesis of ALP, resulting in increased plasma levels.

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