Hepatic Enzymes (AST and ALT)

Prof. Dr. Hedef Dhafir El-Yassin
Objectives:

1. To list hepatic enzymes useful for the differential diagnosis and monitoring of various heptobiliary disorders
2. To discuss the function, localization and clinical significance of aminotransaminases.
3. To differentiate enzyme assays in differential diagnosis of Jaundice
4. To describe Non-alcoholic steatohepatitis (fatty liver)
5. To diagram serum patterns in different liver diseases
• There are two types of enzymes:

1. Enzymes which are normally present inside the hepatocytes released into the blood when there is a hepatocellular damage = markers of hepatocellular damage. (transaminases)

2. Enzymes which are primary membrane bound (plasma membrane or side of hepatocytes) = markers of cholestasis. (ALP)
1. Markers of hepatocellular damage.

Aminotransaminases

- AST catalyzes the reaction:

L-Aspartate + 2-Oxoglutarate $\underset{AST, P-5'-P}{\overset{\text{COO}^\ominus}{\text{COO}^\ominus}}$ $\text{CH}_2$ $\text{CH}_2$ $\text{COO}^\ominus$ $\text{COO}^\ominus$ Oxaloacetate + L-Glutamate
• ALT catalyzes the analogous reaction:

\[
\text{L-Alanine} + \text{2-Oxoglutarate} \rightarrow \text{Pyruvate} + \text{L-Glutamate}
\]
Measurement of AST/ALP ratio is more diagnostic.

- Higher ratio is seen during hepatitis and lower ratio indicates cholestatic disorder.

- AST/ALT ratio of >2 indicates alcoholic hepatitis, especially mAST is elevated.

- Increased ratio of mAST/total AST indicates chronic alcohol abuse irrespective of liver disease.
Causes of Elevated ALT or AST Values in Asymptomatic Patients

A  Autoimmune hepatitis
B  Hepatitis B
C  Hepatitis C
D  Drugs or toxins
E  Ethanol
F  Fatty liver
G  Growths (i.e., tumors)
H  Hemodynamic disorder (congestive heart failure)
I  Iron (hemochromatosis), copper (Wilson's disease) or alpha₁-antitrypsin deficiency
M  Muscle injury: muscle necrosis
Table: Aminotransferase activities in human tissues, relative to serum as unity

<table>
<thead>
<tr>
<th>Tissue</th>
<th>AST</th>
<th>ALT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>7800</td>
<td>450</td>
</tr>
<tr>
<td>Liver</td>
<td>7100</td>
<td>2850</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>5000</td>
<td>300</td>
</tr>
<tr>
<td>Kidneys</td>
<td>4500</td>
<td>1200</td>
</tr>
<tr>
<td>Pancreas</td>
<td>1400</td>
<td>130</td>
</tr>
<tr>
<td>Spleen</td>
<td>700</td>
<td>80</td>
</tr>
<tr>
<td>Lungs</td>
<td>500</td>
<td>45</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Serum</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Aspartate Transaminase (EC 2.6.1.1; L-aspartate:2-oxoglutarate aminotransferase; AST)

- Normal values of AST:  
  male: <35 U/L = <0.60 µkat/L  
  Female:<31 U/L = <0.53 µkat/L

- Half-life = 17 hours.

CAUSES OF RAISED PLASMA AST ACTIVITIES

- Artefactual: Due to in vitro release from erythrocytes if there is haemolysis or if separation of plasma from cells is delayed.

- Physiological: During the neonatal period (about 1.5 times the upper adult reference limit).

- Marked increase (10 to 100 times the upper adult reference limit):
  - Circulatory failure with 'shock' and hypoxia:
  - Myocardial infarction
  - Acute viral or toxic hepatitis.
Alanine Transaminase (EC 2.6.1.2; L-alanine:2-oxoglutarate aminotransferase; ALT)

- Normal values of ALT:
  - Male: <45 U/L = <0.77 µkat/L
  - Female: <34 U/L = <0.58 µkat/L
- Half-life = 47 hours

CAUSES OF RAISED PLASMA ALT ACTIVITIES

- **Marked increase** (10 to 100 times the upper limit of the adult reference range: Acute viral or toxic hepatitis.
- **Moderate increase**:
  - Cirrhosis (may be normal or up to twice the upper adult reference limit):
  - Liver congestion secondary to congestive cardiac failure:
  - Cholestatic jaundice (up to 10 times the upper reference limit in adults)
# Enzyme assays in differential diagnosis of Jaundice

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Pre hepatic</th>
<th>Hepatic</th>
<th>Obstructive</th>
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<tbody>
<tr>
<td>ALT or AST</td>
<td>Usually normal</td>
<td>Marked increase</td>
<td>Increased 100-300IU/L</td>
</tr>
<tr>
<td></td>
<td>500-1500 IU/L</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALP</td>
<td>Normal</td>
<td>Increased slightly</td>
<td>Marked increase</td>
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Non-alcoholic steatohepatitis (fatty liver)

- A liver biopsy should be considered if a chronic liver screen is negative but liver biochemistry remains abnormal (ALT/AST more than twice the Upper Limit of Normal (ULN)) as up to 25% of these patients may have significant liver fibrosis.
- Non-alcoholic steatohepatitis is an increasingly recognized condition associated with an increased BMI, diabetes mellitus and hypercholesterolaemia. Histologically, it mimics alcoholic hepatitis and may present only with elevated serum transaminases.
- It is associated with progression to cirrhosis, so it is important to recognize.
METABOLIC SYNDROME

NAFLD
Non-alcoholic Fatty Live

NASH
Non-alcoholic Steatohepatitis

CIRRHOSIS

LIVER FAILURE

HYPERLIPIDEMIA
Excess fats in the blood such as cholesterol

HEART & VASCULAR DISEASE

CARDIAC FAILURE/STROKE/ARTERIOSCLEROSIS

INSULIN RESISTANCE

TYPE 2 DIABETES

HEART DISEASE/BLINDNESS/CIRCULATION PROBLEMS
Serum Patterns in acute viral hepatitis

Fig 2. Course of serum enzyme activities in acute viral hepatitis
Conclusions:

1. Hepatic markers:
   - markers of hepatocellular damage.
   - markers of cholestasis.

2. The transaminases are enzymes involved in the transfer of an amino group from a 2-amino-to a 2-oxoacid. AST present in cytosol and mitochondria, ALT located in cytosol of liver. These enzymes are more important in assessing and monitoring the degree of liver cell inflammation and necrosis.
### 3. Enzyme assays in differential diagnosis of Jaundice

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4. Non-alcoholic steatohepatitis is an increasingly recognized condition associated with an increased BMI, diabetes mellitus and hypercholesterolemia.
5. Serum Patterns in acute viral hepatitis

![Graph showing serum enzyme activities](image)

Fig 2: Course of serum enzyme activities in acute viral hepatitis
Any questions