Approach to Liver Function Tests

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3 Key Takeaways

- Categorization is key
- Turning the question around: E.g. What causes raised AST?
- Sensitivity and Specificity
What are the functions of the Liver?

- 2 minutes
What are the functions of the LIVER?

- Haematological/Reticuloendothelial System (Recap)
- Nutrition & Metabolism
- Detoxification & Breakdown (Drugs, NH3/Urea, Hormones)
- Bilirubin & Bile handling
- Synthesis: Albumin, Clotting Factors

Angiotensin
3 Components of the LFT

Localizing Source of Pathology

- Hepatic Transport capability – Bilirubin (Total, unconj, conj)

- Cellular Function (Enzymes) – ALT, AST, ALP, GGT

Baseline Liver Function

- Synthetic Function – Albumin, PT
Hepatic Transport Capability

- Localizing source of pathology (Uptake, Conjugation, Excretion)
- Biliary Anatomy (Extra-hepatic, Intra-hepatic – Ducts/Ductules vs. Cannaliculi)
Cellular Function - Enzymes

- ALT & AST
- ALP & GGT
AST

- Mitochondrial Enzyme
- Also in non-hepatic tissues – e.g. heart, skeletal muscle, brain, kidney – raised in myositis/myopathy; RBC – raised in hemolysis
- Enzymes released from damaged cells
ALT

- ALT (Cytoplasmic enzyme)
- More specific for hepatocellular injury
- Enzymes released from damaged cells
AST:ALT

- ALT > AST → Most cases of **hepatocellular injury**
  e.g. Acute Viral Hepatitis

- AST > ALT → *Oxidative (Mitochondria) stress* e.g.
  Alcoholic Liver Disease, Wilson’s
ALP

- ALP is mainly found in
  1. Bile duct (Canalicular & Sinusoidal membrane)
  2. Bone (Osteoblast activity – high bone turnover).
- Other sources - Intestine, Placental
ALP

- When raised in isolation, think of:

1. **Bone**: Healing fractures, osteomalacia, Paget disease of bone, Endocrine: Hyperparathyroidism, hyperthyroidism, Malignancy - bone metastases, multiple myeloma

2. **Liver**: Chronic intra/extra-hepatic cholestasis, infiltrative diseases

3. Intestine: Celiac disease

4. Placenta: 3\(^{rd}\) trimester of pregnancy

5. Physiological: Children and Adolescence
Gamma-Glutamyl Transpeptidase
GGT

- GGT (Microsomal Enzyme): Biliary epithelial cells, hepatocytes, other organs
- Aids in Glutathione regeneration to cope with oxidative stress
- Can be raised in isolation in:
  1. Non-obstructive pattern (Drug/toxin induced released) – e.g. Alcohol intake, Certain drugs – Phenytoin
  2. Fatty Liver Disease/Alcoholic Liver Disease
  3. Other conditions: Pancreatic disease, AMI, Renal Failure, COPD
ALP & GGT

- GGT & ALP (& 5-nucleotidase) rise in parallel in cholestasis (same excretion pathway)
- Main value of GGT is in verifying that ALP elevation is indeed due to biliary disease
- Specificity is increased for biliary disease
Synthetic Function

Components & their utility

1. PT (Factor VII) – Sensitive indicator of **acute & chronic** liver disease

2. Albumin – Assess severity of **chronic** liver disease
Prothrombin Time

- Remember the coagulation pathway? (:  
- Clotting factor with the shortest half life, hence its sensitivity  
- Rule out Vitamin K deficiency in prolonged PT by giving Vitamin K → persistent elevation despite administration indicates severe hepatocellular dysfunction
Serum Albumin

Causes of Hypoalbuminemia

- Decreased production (Chronic Liver Disease, Malnutrition)

- Increased loss (Protein losing enteropathy, Nephrotic Syndrome)
Things you tend to see along with an LFT

- Coagulation – PTT
- Cellular Turnover – LDH
Take Home Learning Points

- Categorization
- Working out an approach to a single lab value
  - Leant in Posting: Pancreatitis causes rise in Amylase
  - Practical Approach: What are the causes of raised amylase?
  - Classify them: Pancreas related, Salivary gland related, Gastrointestinal Causes (Appendicitis, PUD, Peritonitis, IO), Female Reproductive Tract causes, Decreased Metabolism/Clearance (Liver, Renal Failure)
Take Home Learning Points

- Sensitivity & Specificity

- Is this lab value sensitive or specific for pancreatitis?

- What then is its utility?
References

- Kumar & Clarke 8th Edition