Management of abnormal liver function tests (LFTs)

RCGP LEARNING

Basics

What markers of liver function can we measure?

- Standard LFTs = ALT, ALP, bilirubin, albumin, others done separately. Reflex AST testing may be done if ↑ ALT.

AST/ALT	• Enzymes present in hepatocytes – released into blood if hepatocyte injury or death. • ALT is more liver-specific (AST also in muscle and may ↑ in myositis/MI).
ALP	• Made in liver and bone (smaller amounts in guts, kidneys and WBC). • ↑ from liver mainly in cholestatic liver disease, ↑ from bone - Paget's, bony mets, ↓ vitamin D.
GGT	• Present in liver, kidney, gut, prostate and pancreas. • ↑ GGT suggests that an ↑ ALP is from liver not bone.
Bilirubin	• Byproduct of breakdown of haem in haemoglobin. Can ask lab for unconjugated/conjugated split if bilirubin ↑. • ↑ unconjugated – haemolysis, ↑ conjugated – liver or biliary system disease. • Gilbert's disease – normal variant, ↑ unconjugated bilirubin, usually ≤ 85 µmol/L. • ↑ in jaundiced neonate → urgent paeds assessment.
Albumin	• Protein produced in the liver - not a reliable measure of liver function. • ↓ in sepsis, inflammation, nephrotic syndrome, malabsorption and loss of protein via GI tract.
Coagulation	• Clotting factors are made in the liver – coagulopathy usually means >70% liver function lost. • Also due to vitamin K deficiency and warfarin use.

Practicalities of measuring LFTs

When to measure

- Non-specific symptoms (e.g. brain fog, fatigue) – could be viral or autoimmune hepatitis (AIH).
- Signs of chronic liver disease (ascites, peripheral oedema, spider naevi, hepatosplenomegaly).
- Periodic testing in those with autoimmune conditions as associated with AIH – 10% with IBD will have autoimmune cholestatic liver disease.
- Symptoms of liver disease e.g. itch, jaundice.
- To monitor hepatotoxic drugs e.g. methotrexate.
- Alcohol excess – ↓ transaminases with abstention from alcohol can be motivating, though increase isn't proportional to development of progressive fibrosis in those with alcohol excess.
- In those with viral hepatitis.
- Metabolic risk factors for NAFLD/MALSD.

Patterns of raised LFTs

- ↑ bilirubin alone:
  - Usually Gilbert's syndrome.
  - Consider haemolysis if anaemic (check reticulocyte count).
- Hepatic - ↑ ALT/AST but not ALP:
  - Indicates hepatocellular injury.
  - Viral or autoimmune hepatitis, NAFLD/MALSD, alcohol, AIH, drug induced.
- Cholestatic – predominant ↑ ALP and GGT.
  - Primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), liver duct obstruction (e.g. metastatic disease, stones, stricture) and drug-induced cholestasis.
  - Some genetic causes/inherited abnormalities of synthesis/transport of bile acids.
  - Isolated ↑ ALP – consider vitamin D deficiency.

What to do when you are presented with a patient with raised LFTs

Clinical assessment

- Why were the bloods done?
- Are there any symptoms?
- Any signs of liver failure?
- Is the patient from a country which is high-risk for hepatitis B?
- Is the patient acutely unwell or the LFTs bad enough that immediate referral is needed?
  - Jaundice/↓ albumin/↑ INR – same day medics review.
  - Do they fit criteria for urgent suspected cancer/non-specific symptoms pathway referral?

Actions depending on pattern of raised LFTs – more detail here

- Hepatic/cholestatic picture:
  - Repeat with FBC, GGT, hep B/C, autoantibodies, ferritin, transferrin saturation, HbA1c, liver ultrasound.
  - Hepatic - see NAFLD/MASLD NUB if fatty liver shown on ultrasound.
  - Cholestatic – refer as appropriate if any tests abnormal.
  - Both – if all other tests normal/LFTs remain high → refer hepatology.
- Isolated ↑ bilirubin:
  - Repeat with conjugated/unconjugated bilirubin.
  - If level similar and unconjugated → likely Gilbert's → reassure.
  - If conjugated/suggestion of haemolysis → refer.
- Autoantibodies (not diagnostic – refer for confirmation):
  - ↑ AMA – PBC.
  - ↑ ANA/SMA/pANCA - AIH.
  - ↑ pANCA/ASCA – PSC.