Abnormal liver function test pathway

Initial assessment

- History and physical examination
- Alcohol history – AUDIT-C
- Screen for diabetes mellitus and obesity
- Review of medication
- Review of over-the-counter medication and herbal supplements

Non-invasive liver screen

- HBV surface antigen, core antibody and surface antibody
- HCV antibody
- HIV
- Autoantibodies (ANA, SMA, AMA)
- Immunoglobulins
- A1 antitrypsin
- Ceruloplasmin (age <40)
- Ferritin and transferrin saturation
- Coeliac screen

Ultrasound scan

RED FLAGS – URGENT REFERRAL TO LIVER SERVICES

- Jaundice (think acute hepatitis or biliary obstruction)
- ALT >5 x upper limit of normal (ULN)
- ALP >3 x ULN

Consider cirrhosis

- Ascites
- Low platelet count
- Prolonged INR
- Low albumin

Liver screen

Liver screen negative

- Alcohol-related liver disease (ALD)
  - Significant alcohol intake
- Non-alcoholic fatty liver disease (NAFLD)
  - No significant alcohol intake
  - Evidence of fatty liver on USS
  - Risk factors for NAFLD (DM, obesity, metabolic syndrome)

Liver screen positive
REFER TO LIVER SERVICES

Fibrosis assessment

Assessment of fibrosis

- FIB-4 <1.3
- FibroScan <7.8 kPa

MANAGE IN PRIMARY CARE

Assessment of fibrosis

- FIB-4 >2.67
- FIB-4 1.3-2.67 and no FibroScan available
- FibroScan >7.8 kPa

REFER TO LIVER SERVICES

Management in primary care

ALD

- Advice to reduce alcohol to <14 units weekly
- Start Thiamine 100 mg tree times daily and Vitamin B Co-strong two tablets daily
- Refer to local Alcohol Liaison Services if deemed necessary

REPEAT FIB-4/FibroScan EVERY 2-3 YEARS FOR THOSE WHO CONTINUE TO DRINK

NAFLD

- Advice on dietary changes and exercise
- Weight loss >10%
- Optimise DM control
- Treat hyperlipidaemia
- Assess cardiovascular risk (QRISK2 score)
- Consider referral to Obesity Services for those with BMI >35 kg/m^2
- Alcohol intake <14 units weekly

REPEAT FIB-4/FibroScan EVERY 2-3 YEARS

Abnormal liver function test pathway

1. Initial assessment

When assessing a patient with suspected liver disease, look for signs of cirrhosis such as jaundice, ascites, splenomegaly, palmar erythema and spider naevi. Patients with jaundice and ascites should be referred urgently to the Liver Services.

When reviewing medication, ask for medication taken in the last 3 months such as antibiotics or NSAIDs. Also ask for over-the-counter medication and herbal supplements, as some of them have been associated with hepatotoxicity.

Screen for alcohol disorders, obesity, diabetes mellitus and features of the metabolic syndrome.

Organise a non-invasive liver screen and ultrasound scan.

2. Interpretation of liver screen

HBV markers:

- HBV surface antigen positive (HbsAg): Patient has HBV infection and should be referred to the Liver Services.
- HBV surface antigen (HbsAg) negative, core antibody (HbcAb) positive and surface antibody (HbsAb) positive: Patient does not have HBV infection. Markers consistent with previous HBV exposure and immunological clearance (natural immunity). No indication for referral to Liver Services.
- HBV surface antigen (HbsAg) negative, core antibody (HbcAb) negative and surface antibody (HbsAb) positive: Markers consistent with previous HBV vaccination.

HCV antibody positive (HCV IgG): Patient likely has chronic hepatitis C and should be referred to the Liver Services. Patients who were treated for HCV and cleared HCV, will continue to be HCV IgG positive.

Patients with positive ANA and/or SMA and elevated IgG may have autoimmune hepatitis. These patients will typically have elevated ALT/AST.

Patients with positive AMA and elevated IgM may have primary biliary cholangitis. These patients typically have elevated ALP.

Low A1 antitrypsin is a rare cause of chronic liver disease. Some of these patients may also have lung disease (emphysema).

Low caerulopasmin may suggest Wilson's disease in a young patient. This test should only be performed in patients who are <40 years.

High ferritin levels in combination with high transferrin saturation may suggest haemochromatosis. Please note that patients with NAFLD and ALD may also have elevated ferritin levels but the transferrin saturation in these cases is usually normal.

Patients with coeliac disease may have mildly abnormal liver function tests.

PLEASE REFER ALL PATIENTS WITH A POSITIVE LIVER SCREEN TO LIVER SERVICES – IT IS VERY IMPORTANT THAT YOU INCLUDE ALL RESULTS OF PREVIOUS INVESTIGATIONS IN YOUR REFERRAL LETTER

3. Negative liver screen

- Patients with negative liver screen and history of alcohol excess are likely to have alcohol-related liver disease (ALD).
- Patients with negative liver screen, no history of alcohol excess, evidence of fatty liver on USS and metabolic risk factors (diabetes mellitus, obesity, features of the metabolic syndrome) are likely to have non-alcoholic fatty liver disease (NAFLD).

Patients with ALD/NAFLD typically have ALT <200 IU/L. If ALT is higher >200 IU/L consider other or coexisting disorders.

Patients with negative liver screen who do not fall into the above categories should be referred to the Liver Services as may have other unrecognised forms of liver disease.

4. Assessment of fibrosis

For patients with ALD or NAFLD, it is important to assess the extent of liver fibrosis prior to considering referral to Liver Services.

Assessment of fibrosis can be performed non-invasively with either serum biomarkers or transient elastography (FibroScan). FibroScan is more reliable, and if available in the community, should be preferred. Patients who have a FibroScan reading (liver stiffness measurement) <7.8 kPa are unlikely to have advanced fibrosis and can be managed in the community. Patients with LSM >7.8 kPa should be referred to the Liver Services as they are likely to have more advanced stages of fibrosis.

FIB-4 can be easily calculated if FibroScan is not available. A FIB-4 <1.3 is consistent with no significant fibrosis. These patients can be managed in the community. Patients with FIB-4 >2.67 are likely to have more advanced fibrosis, and should be referred to the Liver Services.

For intermediate FIB-4 1.3-2.67, refer for FibroScan if this available, and follow above pathway. If FibroScan is not available, the safest option is to refer to the Liver Services for further assessment.

5. Management in primary care

ALD:

- Educate patients on safe alcohol intake – consider brief interventions.
- Some patients may need referral to local Alcohol Liaison Services.
- Start Thiamine 100 mg tree times daily and Vitamin B Co-strong two tablets daily.

NAFLD:

- Educate patients on lifestyle modifications – see patient leaflet ‘Improving your diet and lifestyle. Advice for patients with NAFLD’

- Weight loss of at least 10%. Smaller weight loss is unlikely to be beneficial in NAFLD.
- Consider referral to Obesity Services for those with BMI >35 kg/m^2
- DM control should be optimised.
- Hyperlipidaemia should be treated irrespectively of CVD risk. Statins are not contraindicated in NAFLD or other forms of liver disease.
- Patients with NAFLD are at risk of CVD, and CVD is the main cause of mortality in this population. Assess CVD risk using QRISK2.
- Alcohol intake should be kept to <14 units weekly.
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6. Re-assessment of fibrosis

All patients managed in primary care should have repeat assessment of fibrosis every 2-3 years. Patients at high risk for progression are:

- ALD who continue to consume excessive amounts of alcohol.
- NAFLD who have DM, are obese (BMI >30 kg/m^2) and those who have several features of the metabolic syndrome.

Refer to the Liver Services if they meet fibrosis criteria.

IT IS VERY IMPORTANT THAT YOU INCLUDE ALL RESULTS OF PREVIOUS INVESTIGATIONS IN YOUR REFERRAL LETTER