NHS
Southampton City
Clinical Commissioning Group

Liver Guidance (Primary Care)

Referral | Pathway | Guidance

List of Contents

Key Messages for this Pathway

- Abnormal LFTs need to be investigated
- Normal LFTs does not exclude liver disease (index of suspicion)
- Advanced liver disease due to any aetiology leads to cirrhosis
- Three most common causes for liver disease are preventable
  - Alcohol
  - NAFLD
  - Viral hepatitis

Background Information

AIM:

- Allow clinicians to make a diagnosis and identify the aetiology for liver disease
- Assess for advanced liver disease to allow referral to hepatology
- Allowing behaviour advice and treatment (where possible) before developing advanced liver disease
- Trying to make a difference to the outcome and statistics (death from liver disease continues to rise)

Consider:

- Everyone who dies of (chronic) liver disease has passed through an earlier stage of liver damage and scarring (fibrosis)
- Early fibrosis is reversible where intervention is possible
- The huge majority of these patients are in the community and are often asymptomatic

Looking for liver problems in primary care:

- **Alcohol:** Alcohol Use Disorders Identification Test C (AUDIT-C) for identification
- **Fat:** Weights and measures, diabetes, BMI >30, metabolic syndrome
- **Viruses:** Test for HBV surface antigen and HCV IgG (there are patients who remain undiagnosed)

Referral pathway:

- Emergency admission via medical registrar/acute medical unit
- Urgent or routine clinic referral
- Advice and guidance

Clinician Information

Non-alcoholic fatty liver disease (NAFLD): assessment and management (2016) NICE NG49

https://pathways.nice.org.uk/pathways/cirrhosis

AUDIT-C https://patient.info/doctor/alcohol-use-disorders-identification-test-audit

British Liver Trust Patient Guides https://www.britishlivertrust.org.uk/publications/download-publications/

Patient Information

- Alcohol Guidance – 'know your numbers'
- Alcohol: https://www.nhs.uk/oneyou/for-your-body/drink-less/
- Helpful tips on how you can improve your health by making changes to your drinking
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- British Heart Foundation – 'Get active, stay active'
- NHS LiveWell – Weight management advice
  https://www.nhs.uk/live-well/healthy-weight/start-the-nhs-weight-loss-plan/
- Includes a 12-week self-led online, weight-loss programme
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Applications:

- Drinkaware App – allows patients to calculate and track weekly units. Free to download on apple or android

Liver History and Examination

Risk factors: Alcohol, metabolic syndrome, drugs, blood transfusions, tattoos, sex, travel/living abroad
PMH: T2DM, insulin resistance, hypertension, dyslipidaemia, central adiposity – all cardiovascular risk factors
FH: Autoimmunity and related conditions
Medications: Prescribed or otherwise
Other: Odd hobbies (pets, water sports), occupation, exposure to jaundiced persons
Assessment: Jaundice or signs of chronic liver disease.

Medication Review

If a drug-related cause is suspected, further information is available from Medicines Information Team at UHS (tel. 023 8079 6908)

Almost any medication can cause an elevation of liver enzymes:
nonsteroidal anti-inflammatory drugs (NSAIDs), antibiotics, statins, anti-epileptic and antituberculous drugs, herbal preparations and illicit drugs, amiodarone, methotrexate, diltiazem, glucocorticoids, tamoxifen, phenytoin, barbiturates, statins

STATINS
Abnormal LFTs on statins relate to physiology and planned pharmacological effect. A raised ALT on a statin often decreases over time, often doesn't recur after reintroduction or re-escalation after dose reduction. Don't avoid them.

Only consider stopping statins if liver enzyme levels double within 3 months of starting statins, including in people with abnormal baseline liver blood results

Primary Care Liver Screen

Use Liver Screen panel to request on ICE
A standard primary care liver screen should be made up of:

FBC
Clotting
Liver profile
GGT (only use if ALP raised to determine whether ALP is from liver or bone origin – an isolated incidental finding of a GGT <100 with normal ALP should be considered as insignificant)
HbA1c
Fasting lipid profile
Triglicerides

Plus NILS – see below

Hepatitis B and C
- Immunoglobulins
- Autoantibodies
- High ferritin

If any NILS are positive a referral to hepatology is indicated
- Autoimmune hepatitis could be considered if ALT and IgG raised but negative autoantibodies
- NILS negative excludes:
  - Sero-positive autoimmune hepatitis
  - Hep B and C viral hepatitis
  - Hereditary haemachromatosis

Do not use routine liver panel blood tests to rule out NAFLD or advanced liver fibrosis/cirrhosis

ALT Interpretation

- Consider non-hepatic cause for abnormal ALT:
  - Thyroid disease
  - Muscle disease, e.g. polymyositis, heavy exercise
  - Coeliac disease
- If ALT <3 ULN and NILS negative no further action needed

Establish Source of Raised ALP/Interpretation of GGT

- ALP raised BUT normal GGT – indicates ALP is not liver related – consider:
  - Vitamin D deficiency
  - Bone disease
  - Third trimester pregnancy
- ALP varies with age (rapidly growing adolescents have up to 2-fold increase)
- ALP raised but <2 ULN with negative NILS, in a non-drinker should be considered an incidental finding
- If GGT <100 and all other LFTs are normal this should be considered an incidental finding

Incidental Finding of Fatty Liver on Ultrasound

This should not be considered normal
All patients need a primary care liver screen (including NILS) and assessment (weight/AUDIT-C) even if LFTs are normal.
Appropriate lifestyle advice should be given.

Alcohol-related Liver Disease

- 24% of the English population (33% of men and 16% of women) consume alcohol in a way that is potentially or actually harmful to their health.
- Of the 1 million people aged between 16 and 65 who are alcohol-dependent in England, only about 6% per year receive treatment

Presentation:
Craving, tolerance, a preoccupation with alcohol and continued drinking in spite of harmful consequences (to health and wellbeing)

Diagnosis:
- Opportunistic screen with AUDIT tool
- Simple biological measures e.g. liver function tests are poor indicators of the presence of harmful or dependent drinking
- Assessment of the severity of alcohol misuse is important because it points to the treatment interventions required
- AUDIT >10: ELF test to assess for advanced fibrosis
- If AUDIT C is not performed >30 unit alcohol consumption per week or ELF >9 refer for community Fibroscan.

Treatment:
- Mild dependence – may not require assisted withdrawal
- Moderate dependence – community-based assisted alcohol withdrawal
- Severe dependence – assisted alcohol withdrawal, typically in residential setting or planned admission to secondary care
- AUDIT >15 – comprehensive assessment for all adults in specialist alcohol treatment services
- Acamprosate – start treatment as soon as possible after assisted withdrawal

Thiamine for people at high risk of developing, or with suspected, Wernicke's encephalopathy. Stop after 6 months if the patient has abstained
from alcohol, but please continue if alcohol consumption continues
- · Vitamin B co strong for 3 months only to replace niacin

Prognosis:
- Liver disease-related morbidity and mortality: HCC, variceal bleed, ascites, encephalopathy
- Cardiovascular disease, neuropathy, cognitive impairment

Non-alcoholic Fatty Liver Disease (NAFLD)

Normal to <3 x upper limit of normal (ULN) ALT or AST: 50% turn out to be due to fatty liver. 33% of adults are obese, 90% of patients with diabetes and obesity have NAFLD. It is the highest single cause of liver disease. All age groups (including paediatrics) increases risk of cardiovascular disease.

Spectrum of disease:

- Fat in the liver (steatosis – NAFLD - >30% of liver contains fat)
- Fat-related inflammation in the liver (steatohepatitis – NASH)
- NASH-related advanced fibrosis
- NASH-related cirrhosis

Presentation:
Usually incidental finding: Just about anything that might make you check their LFTs or request an ultrasound. High-risk groups: metabolic syndrome, obese, diabetes mellitus, hypertension, dyslipidaemia. 'Sentinel condition' to trigger health interventions – at risk of developing cardiovascular disease, diabetes, cancer. Shift from diagnosis of exclusion to positive diagnosis with basic liver screen to exclude co-factors.

Diagnosis: Absence of alcohol history (≤14 units a week), absence of other aetiologies
Primary care test: ELF test
Refer to Community fibroscan if ELF >9
Secondary care tests: fibro-scan with CAP, MRI liver scan, liver biopsy

Treatment:

- Weight loss and exercise, follow BHF guidelines
- Address co-factors (alcohol, good DM control, treat dyslipidaemia, etc.)
- Bariatric surgery if motivated
- Await trials of new agents

Prognosis:
Main risk to mortality and morbidity due to:

- CVS disease
- Increased risk of cancer (including hepatocellular carcinoma)
- Development of diabetes
- Progression to liver cirrhosis

ELF – Enhanced Liver Fibrosis Score

The ELF score combines quantitative serum concentration measurements of three fibrosis markers (TIMP-1, PIIINP and HA) to a single value. These extracellular matrix (ECM) markers show good correlations with fibrosis stages in chronic liver disease.

1. tissue inhibitor of metalloproteinases 1 (TIMP-1),
2. amino-terminal propeptide of type III procollagen (PIIINP)
3. hyaluronic acid (HA)

Liver fibrogenesis represents the uniform response of the liver to toxic, infectious or metabolic agents and is characterised by an increased synthesis and altered deposition of newly formed extracellular matrix (ECM) components

NICE suggest that: consider using the enhanced liver fibrosis (ELF) test in people who have been diagnosed with non-alcoholic fatty liver disease (NAFLD) to test for advanced liver fibrosis:

- diagnose people with advanced liver fibrosis if they have:
  - an ELF score of 9 or above
  - refer adults and young people diagnosed with advanced liver fibrosis to community Fibroscan clinic
  - If Fibroscan confirms advanced fibrosis patients will be accepted under hepatology care at University Hospital SouthamptonS
- explain to people with an ELF score below 10.51 that:
  - they are unlikely to have advanced liver fibrosis and reassessment for advanced liver fibrosis every 3 years for adults and every 2 years for children and young people is sufficient for regular monitoring and no interim tests are needed
- offer retesting for advanced liver fibrosis for people with an ELF score below 10.5:
  - every 3 years to adults
  - every 2 years to children and young people
- consider using ELF for retesting people with advanced liver fibrosis

If ALT at 6 months <3 x ULN and no diabetes, metabolic syndrome and non-hepatic causes for ALT excluded consider review at 3 years.

What happens to those who get referred?

If advanced liver fibrosis is confirmed at community Fiborscan clinic these patients will be accepted under hepatology care at UHS
In secondary care, referred patients will be accessed for cirrhosis
Screening programmes patients with cirrhosis: Hepatocellular carcinoma, varices, liver transplant assessment
Management of co-existent liver problems

Fibro-scanning: Principles

Specific to the liver, a little like an ultrasound.
An elastic shear wave is created by vibration of a probe against the liver between the ribs. This vibration travels through the liver. Velocity of vibration is proportional to stiffness and inversely proportional to elasticity which was correlated with liver biopsy findings during development of the device.
Liver stiffness is measured in kPa.
Very good at providing reassurance with normal results.
Very good at diagnosing cirrhosis and hence targeting screening programme
Less helpful to assess severity of fibrosis in the mild to moderate range of fibrosis therefore additional investigations performed: ELF test in primary care; MRI liver, liver biopsy in secondary care

Red Flags

Suspected malignancy
Jaundice
Consider acute hepatitis / biliary obstruction

- ALT 5x upper limit of normal
- ALP 5x ULN

Consider cirrhosis

- Low platelets
- Persistent low albumin
- High INR
- Ascites
- Encephalopathy
- Haematemesis

Sepsis
Clinical judgement needed – admission via medical registrar/2WW/urgent clinic referral

Dr M. Mathew and Dr J. Patel

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