Nottingham and Nottinghamshire Adult Liver Disease Guideline V37: September 2021

Raised ALP with normal GGT
Consider Bone Disease & Vitamin D levels

Normal LFTs : Patients at increased risk of Advanced Liver Fibrosis or Liver Cirrhosis (Obesity and Type 2 Diabetes or Hazardous Alcohol use) will be systematically invited for assessment on a Primary Care Network basis. Patients with known intermediate Fibroscan results can be referred for an interval scan after 3-5 years.

Isolated raised Bilirubin with normal ALT/ALP and Hb
Consider Gilbert's Syndrome*

Suspected Synthetic failure:
Jaundice, low albumin, prolonged INR
OR
Suspected Malignancy:
weight loss, jaundice, marked cholestasis

Raised ALP* with raised GGT

Raised ALT

Request Immunoglobulins and Autoantibodies*

Request Viral Hepatitis screen*, Immunoglobulins*, Autoantibodies, ANA*, Ferritin, Transferrin Saturations, Coeliac, TFT, Liver Risk Assessment

Request Ultrasound Scan Liver

ALT >250*

Risk factors* for Non-Alcoholic Fatty Liver Disease (NAFLD)

Alcohol use >35 units female or >50 units male or full AUDIT >19

Metastases or mass identified

Abnormal USS

Normal USS

ICE Request: NAFLD Liver Risk Assessment (FIB4/Fibroscan/ELF cascade)

ICE Request: Alcohol Related Liver Risk Assessment (ELF test/ Fibroscan)

2 Week Wait Hepatobiliary Surgery or Hepatology referral

Referral or Advice from relevant speciality

Referral or Advice Hepatology / Gastroenterology

- FIB4 Low (Under65 years < 1.3)(65years or Over < 2): Reassess risk in 3 years
- FIB4 Indeterminate : Lab will process ELF test or book Fibroscan
- FIB4 High (Any Age >3.25) : Refer Hepatology or Gastroenterology
- Fibroscan ≤ 8 or ELF < 10.51: Reassess risk in 3 years
- Fibroscan >8 kpa ≤15 kpa : Consider referral, address risk factors, reassess 3-5 years*
- Fibroscan > 15kpa or ELF ≥10.51 : Refer Hepatology or Gastroenterology
- Refer abnormal results as clinically appropriate using the additional notes

Additional Notes

Elevated ALT

The most common explanation for elevated ALT is fatty liver disease driven either by diet, metabolism or alcohol and lifestyle advice should be given.

Risk Factors for NAFLD are

- Obesity
- Type 2 Diabetes
- Hypertension
- Dyslipidaemia
- Ischaemic Heart Disease
- Family History of hypertension/IHD/type 2 diabetes
- Hypothyroidism
- PCOS

Patients with isolated ALT rise with these conditions it is reasonable to attribute the ALT result to fatty liver disease and arrange no further investigations, unless they have an intermediate or high FIB4 score or have features on USS or examination of cirrhosis. Patients with persistently raised ALT without risk factors, harmful alcohol use or another cause should be considered for referral and investigation.

Harmful alcohol use

NICE define this as:

- Men who drink over 50 units of alcohol per week and have done so for a minimum several months
- Women who drink over 35 units of alcohol per week and have done so for a minimum several months
- Full AUDIT score >19

For those with alcohol dependence / alcoholism they need to be willing to consider reducing their drinking. For those with excessive drinking there is good evidence that brief intervention is helpful in changing behaviours. These should be included in the consultation when discussing the scan. Consider referral to Alcohol Services.

Review Date April 2024

FIB-4

This is a Liver Fibrosis Score calculated using ALT, AST and Platelet counts.

It has an age modified cut off range as endorsed by the British Society of Gastroenterologists.

***Fibroscan 8-14.99kpa and referral**

Patients falling into this category may have significant liver fibrosis or cirrhosis. Look for clinical features of cirrhosis (including splenomegaly, thrombocytopenia). The decision to refer therefore needs to factor in other severe co-morbidities or limited life expectancy and consider whether the patient would be willing to accept further invasive investigation (such as liver biopsy) or is seeking further information about their liver disease and future liver risk.

These patients will likely benefit from aggressive management of risk factors. Weight loss of 5% and reductions in alcohol to safe levels have been shown to arrest the progression from Advanced Liver Fibrosis to Liver Cirrhosis. Consider an interval Fibroscan after 3-5 years.

***ELF testing**

Fibroscan and ELF test (Extended Liver Fibrosis Score) are clinically equivalent tests and will be selected depending on local availability. ELF testing is a blood test – no further blood samples are required beyond those take for NAFLD screen. Refer appropriate patients with ELF scores of ≥ 10.51 to secondary care for assessment (NG49).

***Immunoglobulins and liver autoantibodies**

To identify patients with auto-immune hepatitis please refer patients with abnormal LFTs and either a positive liver antibody (anti-Smooth muscle actin sub-type / anti-LKM1) or strongly positive ANA (1: 1600). Immunoglobulin G (IgG) is commonly raised in this condition.

Positive anti-mitochondrial antibody is strongly associated with primary biliary cholangitis and is often seen with elevated IgM. Patients with this condition may have normal LFTs but still be symptomatic. If asymptomatic and LFTs normal recommend monitoring LFT every 2 years and refer when LFTs abnormal or patient develops symptoms of fatigue or itch

A polyclonal rise in Immunoglobulins may occur in patients with Cirrhosis.

Weakly positive ANA or non-specific antibodies do not prevent Fibroscan referral if otherwise indicated.

*** Isolated elevated ALP**

Alkaline phosphatase is produced predominantly by the liver and bone; however gut, pancreas, kidney and placenta are alternative sources and mildly elevated ALP should be evaluated in the context of co-morbidities and underlying indication for LFT measurement. Where other LFTs are normal GGT will automatically be quantified by the NUH pathology laboratory when ALP ≥ 160 U/L.

***Ferritin**

Note the commonest cause of raised ferritin is fatty liver. Ferritin is also an acute phase protein and rises in acute liver injury and systemic inflammation. If no acute cause is obvious request fasting transferrin saturation on 2 separate occasions. Fasting transferrin is raised if >55% in males and >50% in females.

If you have a raised ferritin of <1000 and normal fasting transferrin saturation assume fatty liver – proceed to Fibroscan if indicated.

If ferritin > 1000 &/or transferrin saturation is persistently raised refer to hepatology and in the meantime request HFE mutations blood test

to investigate haemochromatosis.

Hepatitis B

Refer all patients with positive hepatitis B surface antigen (HBSAg) – screen for HIV before referral.

Request HBV DNA measurement prior to referral

***Hepatitis C**

Hepatitis C Ab positive indicates exposure to Hepatitis C. Request HCV RNA and genotype screen (to confirm active infection) and HIV screen.

Refer all patients with HCV RNA present.

Caeruloplasmin and Wilsons Disease

Only test if under 40 years old and Wilsons disease is suspected – i.e odd neurological or behavioural symptoms. The commonest reason for low caeruloplasmin is NAFLD rather than Wilsons disease. If low result, send 24 hour urine collection for urinary copper prior to considering referral.

Gilbert's Syndrome

This is a common cause of isolated hyperbilirubinemia. No treatment is necessary other than informing and counselling the patient.

Governance

This Pathway is drawn from the British Gastroenterological Society Guideline on the Management of Abnormal Liver Blood tests, 2017; NICE guidance NG 49,50 and MIB2016.

This pathway has been approved and endorsed for use in Primary Care by the Nottingham University Hospitals 10th sept 2021, Divisional Leadership Team meeting

This pathway has been approved and endorsed by the Sherwood Hospital Trust Gastroenterological Group for use in Primary Care 21/04/2021