Liver Disease

Presenter: Dr. Milta Little
Disclosure Statement: I have nothing to disclose.

Objectives: By the end of the session, participants will be able to…

- List the initial studies to evaluate potential liver disease
- Describe an algorithm for evaluating the underlying causes of liver pathology
- Formulate a differential diagnosis based on liver blood test results
- List and describe the management of adverse events in liver cirrhosis

Expected Outcomes (Desired change in practice):

- Follow an algorithmic approach to liver disease evaluation in the NH
- Improve outcomes for people living with liver disease in NH

Article for Review: **Newsom PN, et al. Guidelines on the management of abnormal liver blood tests. Gut 2018; 67:6-19.**

Additional articles used:
UpToDate Cirrhosis in adults: Overview of complications, general management, and prognosis
Campbell KA, Trivedi HD, and Chopra S. Infections in Cirrhosis: A Guide for the Clinician. Am J of Med 2021; 134:727-734

Outline for Rapid Fire session

1. Case: liver disease

A 72-year-old woman with past medical history of rheumatoid arthritis, lupus, HTN, HLD, and recurrent CVA has been living in your nursing facility for the past year. Medications include aspirin 81 mg daily, simvastatin 40 mg daily, lisinopril 10 mg daily, amlodipine 5 mg daily, methotrexate 20 mg weekly, and folic acid 1 mg daily. There is no history of alcohol use, recreational drug use, or nonprescription health supplement use; and no family history of liver disease. You are asked to evaluate her for concern of generalized abdominal pain. Labs were obtained and liver chemistries were total bilirubin 0.7 mg/dL, direct bilirubin 0.3 mg/dL, aspartate aminotransferase 125 U/L, alanine aminotransferase 94 U/L, alkaline phosphatase 468 U/L, and international normalized ratio 1.3.
What are your next steps in management?

2. Liver blood testing and interpretation
    a. Basic liver panel: ALT, AP, bilirubin, albumin, GGT, CBC; AST did not improve detection of specific disease but AST:ALT to determine level of fibrosis
    b. When a liver panel should be checked
        i. New non-specific symptoms: fatigue, nausea, anorexia

ii. Signs of liver disease on exam: ascites, edema, spider nevi, HSM
iii. Pre-existing autoimmune disease warrant periodic monitoring
iv. Use of hepatotoxic drugs: carbamazepine, methyldopa, minocycline, macrolide antibiotics, nitrofurantoin, statins, sulfonamides, terbinafine, chlorpromazine and methotrexate
v. Family history of liver diseases – check clinical history in older adults for prior work-up
vi. Presence of risk factors? (obesity, DM, alcohol use)

Research Recommendation 1: Further evidence is required to establish the cost-effectiveness of case finding for NAFLD in high-risk groups before it can be recommended. (level 5, grade D)

c. Interpretation of results (figure 1)

The magnitude or duration of abnormality do not determine clinical significance or need for further eval
Recommendation 2: Abnormal liver blood test results should only be interpreted after review of the previous results, past medical history and current medical condition. (level 5, grade D)

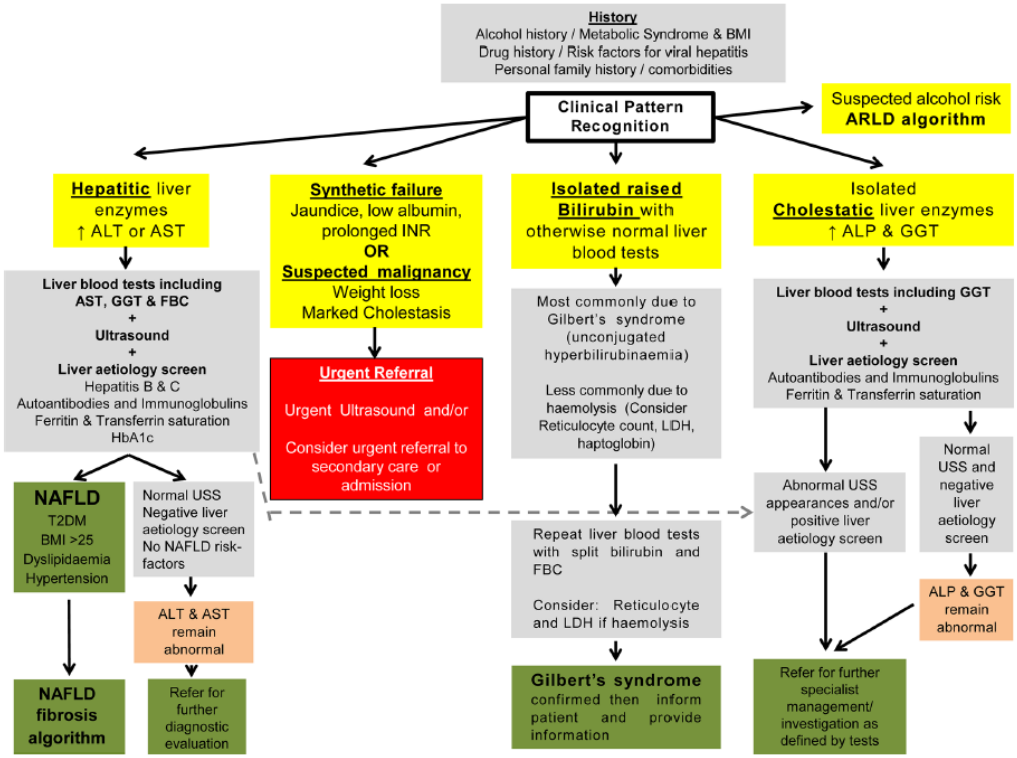

Figure 1 Response to abnormal liver blood tests. This figure details the initial response to abnormal liver blood tests. Boxes in yellow indicate the initial evaluation of the clinical presentation. Patients with marked derangement of liver blood tests, synthetic failure and/or suspicious clinical symptoms/signs should be considered for urgent referral to secondary care (red box). For the remainder, a clinical history alongside evaluation of the pattern of liver blood test derangement will determine choice of pathway and is shown in the grey boxes. A grey box indicates all the tests that should be requested at that stage rather than a hierarchy within it. The presence of metabolic syndrome criteria should be sought to support a diagnosis of NAFLD. For children, the text should be consulted for modification of recommendation. Areas of diagnostic uncertainty are indicated in orange boxes and the decision for repeat testing or referral to secondary care will be influenced by the magnitude of enzyme elevation and clinical context. Green boxes indicate final/definitive outcomes for users of the pathway. *Abnormal USS may well include extrahepatic biliary obstruction due to malignancy, which should result in urgent referral. ALP, alkaline phosphatase; ALT, alanine aminotransferase; ARLD, alcohol-related liver

3. Common etiologies for non-acute abnormal liver blood tests (table 2): Clinical pattern recognition
    a. Isolated raised bilirubin
        i. Gilbert's syndrome most common (elevated total and indirect bili)
        ii. If anemia, consider hemolysis – exclude with reticulocyte count, lactate dehydrogenase, and haptoglobin
    b. Cholestatic – predominantly raised AP and GGT
        i. Common causes include primary biliary cholangitis, PSC, biliary obstruction (stones, strictures, neoplasia, etc), hepatic congestion and drug-induced liver injury
        ii. Isolated raised AP may be from vitamin D deficiency
    c. Hepatic – predominantly raised ALT and AST
        i. Hepatocellular liver injury (hepatitis)
        ii. Viral, non-alcoholic fatty liver disease, drug-induced, autoimmune, alcohol-related liver disease

Table 2 Liver aetiology table for patients with non-acute abnormal liver blood tests

	Standard liver aetiology panel	Extended liver aetiology panel
Viral hepatitis	Hepatitis B surface antigen AND hepatitis C antibody (with follow-on PCR if positive)	Anti-HBc and anti-HBs hepatitis B DNA quantification of hepatitis delta in high-prevalence areas
Iron overload	Ferritin AND transferrin saturation	Haemochromatosis gene testing
Autoimmune liver disease (excluding PSC)	Anti-mitochondrial antibody, anti-smooth muscle antibody, antinuclear antibody, serum immunoglobulins	Anti-LKM antibody and coeliac antibodies (consider ANCA in the presence of cholestatic liver blood tests)
Metabolic liver disease		Alpha-1-antitrypsin level; thyroid function tests; caeruloplasmin (age >3 and <40 years)±urinary copper collection

ANCA, antineutrophil cytoplasmic antibodies; LKM, liver kidney miscrosome; PCR, polymerase chain reaction; PSC, primary sclerosing cholangitis.

4. General approach to NAFLD (table 3 for fibrosis score calculations)

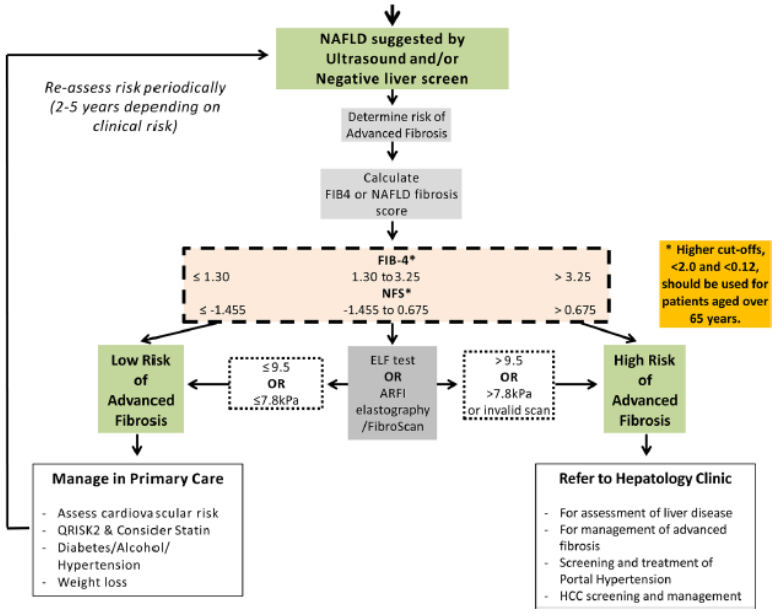

Figure 2 Non-alcoholic fatty liver fibrosis algorithm. For those patients with NAFLD or liver disease of unknown aetiology, the next step

5. Management of cirrhosis complications
    a. Variceal bleeding
        i. Screening EGD for all people with cirrhosis
        ii. Treat with ligation or nonselective beta-blocker (NSBB)
    b. Thrombocytopenia or elevated INR
        i. only treat if invasive procedure or active bleeding
    c. Hepatocellular carcinoma – q 6-month US
    d. Hepatic encephalopathy – clinical monitoring and appropriate deprescribing
    e. Spontaneous bacterial peritonitis (SBP) prevention
        i. high protein diet; judicious (avoid) use of chronic PPI; judicious use of NSBB (bleeding prophylaxis for demonstrated varices only)
        ii. antibiotic prophylaxis for cirrhosis AND a) acute GI bleed; b) ascitic total protein <1.5; b) prior history of SBP
    f. When to refer to hospice? median survival was ≤6 months…
        i. in patients with decompensated cirrhosis and a Child-Pugh score ≥12 or a MELD score ≥21
        ii. in patients with decompensated cirrhosis who had been hospitalized with an acute liver-related illness (e.g., variceal hemorrhage or spontaneous bacterial peritonitis) if the Child-Pugh score was ≥12 or the MELD score was ≥18