MNT of Liver Diseases

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Key Liver Functions:

- **Detoxification**: Removes harmful substances, toxins, and drugs (e.g., alcohol) from the blood.
- **Metabolism & Digestion**: Produces bile to break down fats and processes carbohydrates into energy (glycogen storage and glucose release).
- **Protein Synthesis**: Creates important proteins such as albumin (to transport nutrients) and blood clotting factors.
- **Storage**: Stores vitamins (A, D, E, K, B12), iron, and glycogen.
- **Immune System Support**: Removes bacteria and viruses from the blood.

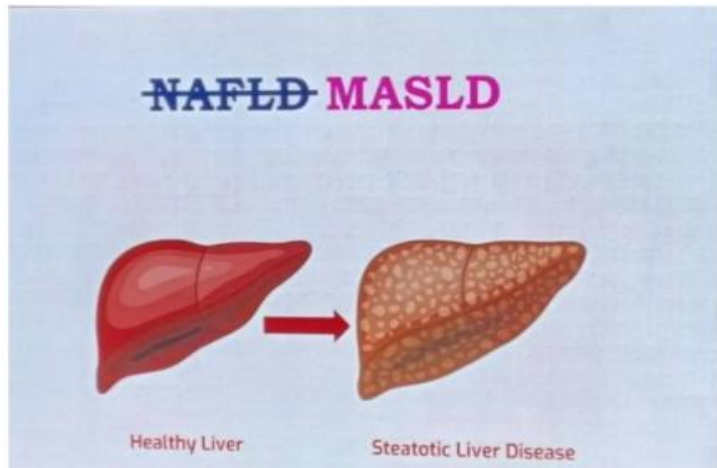
DISEASES OF LIVER

- Liver disease progresses slowly.
- Its primary symptom, fatigue, often goes unnoticed.
- At every step of the way, education and support are critical elements of treatment.
- Health care providers should emphasize the need to preserve remaining liver function, as healthy liver tissue can proliferate, improving prognosis.
- Preventing additional damage is the principal means of avoiding liver failure or transplantation.

Common liver diseases

- **Fatty Liver**
- **Hepatitis**
- **Cirrhosis**

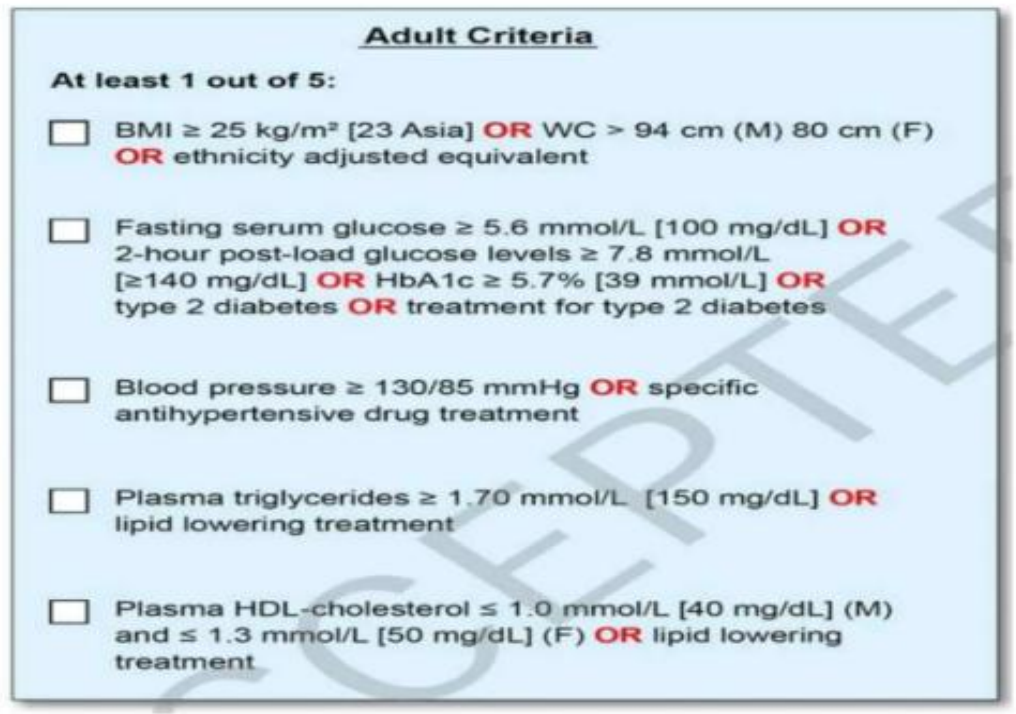
Metabolic dysfunction Associated Steatotic Liver Disease(MASLD).



NOMNICULTURE

- MASLD defined as presence of hepatic steatosis with one or more cardiometabolic risk factors (CMRF), and no other identifiable cause of steatosis.
- Similarly NASH was replaced by MASH (Metabolic dysfunction Associated Steatohepatitis) and NAFL was replaced by MAFL (Metabolic dysfunction associated steatotic liver).
- Patients with hepatic steatosis, CMRFs and alcohol use are classified as having MetALD.
- Patients with steatosis consuming alcohol in excess of 50g/day in females or 60g/day in males or weekly equivalent are classified as Alcohol associated liver disease(ALD).

CRITERIA FOR MASLD

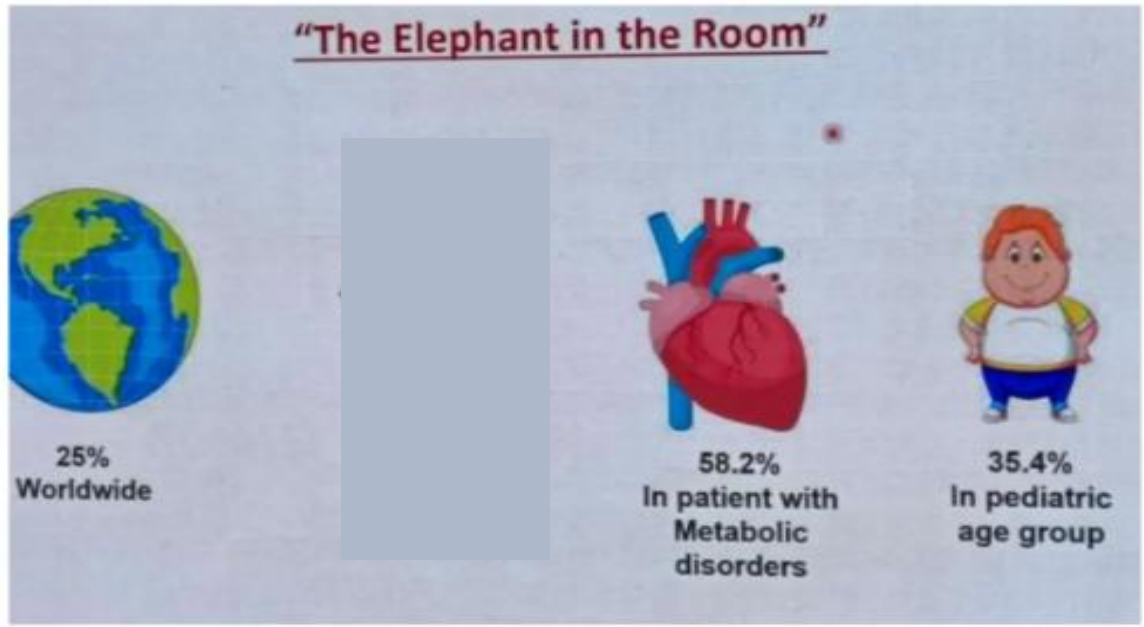


Adult Criteria

At least 1 out of 5:

- ☐ BMI ≥ 25 kg/m² [23 Asia] **OR** WC > 94 cm (M) 80 cm (F) **OR** ethnicity adjusted equivalent
- ☐ Fasting serum glucose ≥ 5.6 mmol/L [100 mg/dL] **OR** 2-hour post-load glucose levels ≥ 7.8 mmol/L [≥140 mg/dL] **OR** HbA1c ≥ 5.7% [39 mmol/L] **OR** type 2 diabetes **OR** treatment for type 2 diabetes
- ☐ Blood pressure ≥ 130/85 mmHg **OR** specific antihypertensive drug treatment
- ☐ Plasma triglycerides ≥ 1.70 mmol/L [150 mg/dL] **OR** lipid lowering treatment
- ☐ Plasma HDL-cholesterol ≤ 1.0 mmol/L [40 mg/dL] (M) and ≤ 1.3 mmol/L [50 mg/dL] (F) **OR** lipid lowering treatment

PREVALENCE OF NAFLD



PREVALENCE

- NAFLD is the most common cause of Chronic liver disease in US and worldwide.
- NAFLD risk is 4-10 times higher in patients with metabolic syndrome.
- NAFLD is further classified as NAFL (isolated steatosis) and NASH (steatosis complicated by liver cell injury and accumulation of inflammatory cells).
- Around 20-25% of NAFLD patients develop NASH.
- Around 6% of NASH patients develop cirrhosis and 1-2% individuals will progress to hepatocellular carcinoma.
- NAFLD is more common in males than females in premenopausal age group, followed by later peak in postmenopausal women.

Prevalence in Iraq is high, reflecting a ~32% prevalence rate found across the Middle East.

ETIOPATHOGENESIS

- RISK FACTORS

COMMON RISK FACTORS	OTHER RISK FACTORS	GENETIC POLYMORPHISM
Obesity	Hypothyroidism	PNPLA3 gene variants
Diabetes mellitus	Obstructive sleep apnea	
Dyslipidemia	Hypopituitary, hypogonadism	
Metabolic syndrome	Alterations in gut microbiome.	
	PCOD	

PRODUCE PROTEIN IN THE LIVER AND FAT CELL THAT REGULATE FAT METABOLISM

ALTERNATIVE CAUSES OF HEPATIC STEATOSIS

MICROVESICULAR STEATOSIS	MACROVESICULAR STEATOSIS	DRUGS CAUSING STEATOSIS
Pregnancy - AFLP	Chronic viral hepatitis – HCV	Tetracyclines
Reyes syndrome	Wilsons disease	Valproate
Eclampsia, HELLP syndrome	NASH	Zidovudine
Tetracyclines		Amiodarone, bleomycin
Valproate toxicity.		Estrogens, steroids
Alcohol		Metals like chromium barium antimony
Acid lipase deficiency.		

THEORIES OF CAUSATION

- TWO HIT HYPOTHESIS
- First hit in the form of sedentary lifestyle, obesity, high fat diet, diabetes mellitus, insulin resistance lead to accumulation of fats within hepatocytes.
- Obesity lead to altered gut microbiota and increased hepatic exposure to gut derived products as well adipokines together are responsible for insulin resistance.
- Second hit in the form of hepatocyte lipotoxicity (due to diacylglycerols, fatty acids), oxidative stress (reactive oxygen species) lead to activation of inflammatory cytokines and hepatocyte cell death.
- This lead to activation of myofibroblasts, progenitor cells that lead to progressive accumulation of wound healing cells, fibrous matrix, abnormal vasculature resulting in irreversible fibrosis.
- Cirrhosis and hepatocellular carcinoma are the potential outcomes of NASH.

CLINICAL FEATURES

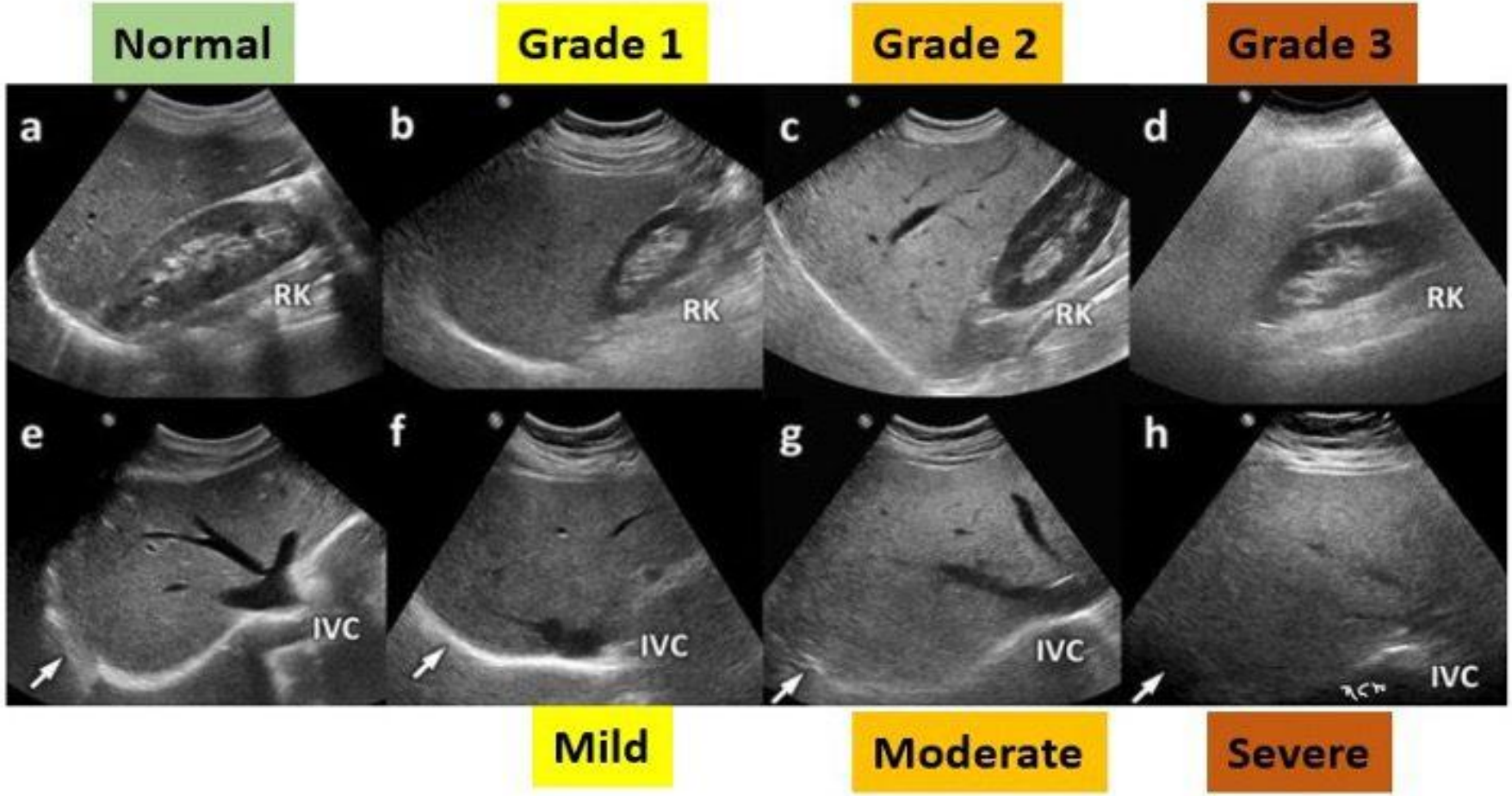
- Most patients with NAFLD are asymptomatic
- Some present with vague RUQ abdominal pain fatigue malaise.
- Hepatomegaly can be found on abdominal examination.
- Signs of chronic liver disease like splenomegaly palmar erythema spider angiomata ascites can be seen in some patients.
- Most of the patients will be associated with obesity diabetes hypertension dyslipidemia cardiovascular disease.

DIAGNOSIS

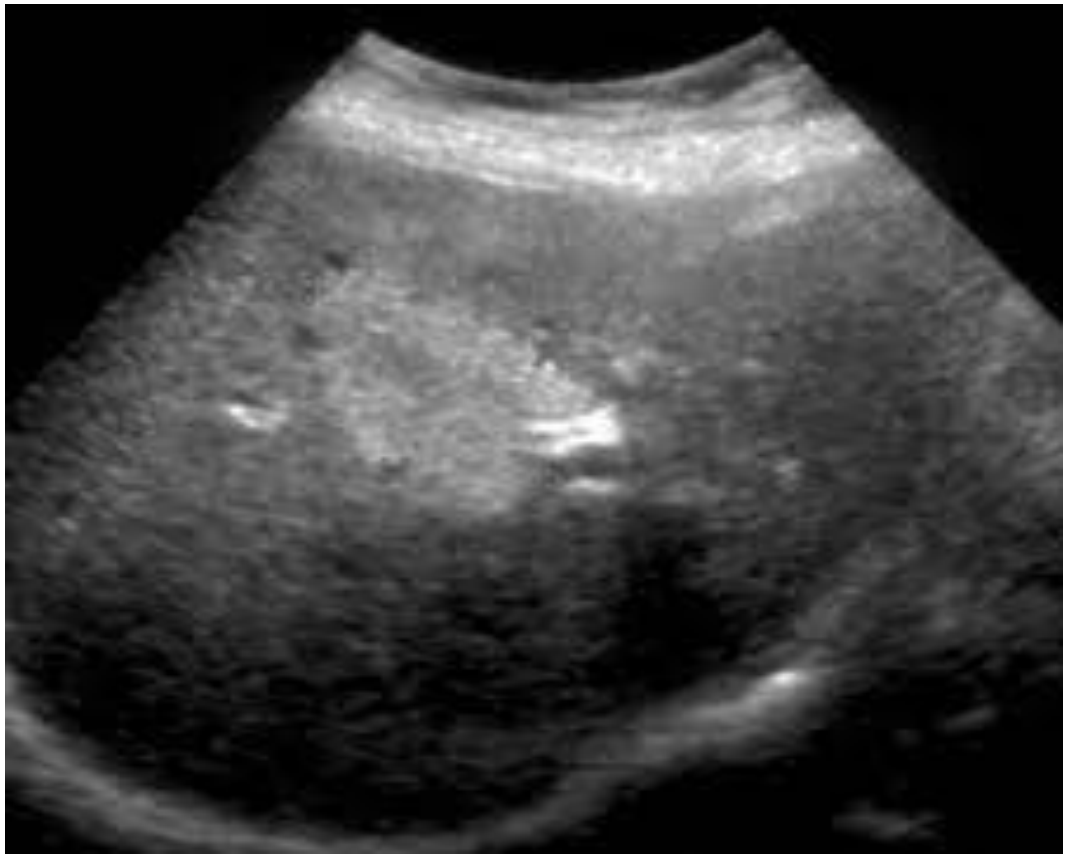
- BIOCHEMICAL PARAMETERS
- LFT shows ALT and AST elevations 2 to 5 times upper limit of normal (30-150IU/L).
- AST/ALT ratio is less than 1 unlike that of alcoholic liver disease.
- Serum ferritin can be elevated
- S Bilirubin albumin prothrombin time are usually normal in NAFLD except in patients with cirrhosis.
- In Isolated fatty liver (NAFL) liver may not be enlarged and aminotransferases and LFT may be completely normal.
- Risk factors for NAFLD should be evaluated – body mass index, diabetes, lipid profile, PCOD, thyroid function tests etc.

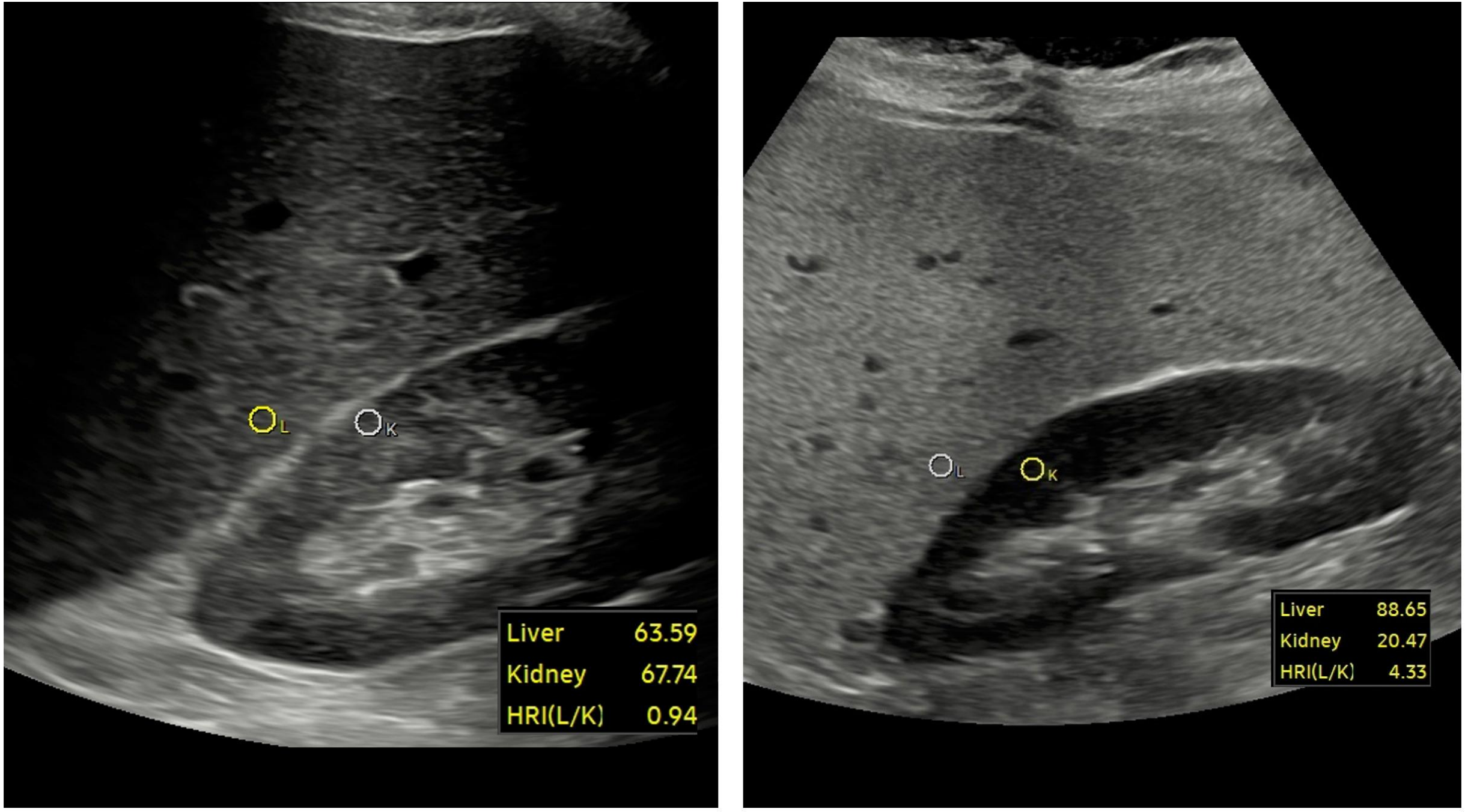
- Other causes of fatty liver like viral hepatitis autoimmune hepatitis Wilson's disease hemochromatosis etc should be excluded.
- NAFLD can coexist in patients with HCV infection
- Serum and hepatic iron levels to be checked to rule out hemochromatosis
- Serum levels of copper ceruloplasmin to rule out Wilson's disease
- About one fourth of patients with NAFLD have antinuclear antibodies positivity in low titres (<1:320).

- IMAGING STUDIES
- Ultrasound abdomen is the first line imaging test
- USG shows fatty liver (macrovesicular steatosis)
- USG cant differentiate between NAFLD and NASH and cant detect fibrosis.
- CT and MRI enhances sensitivity for liver fat detection but adds expense.


Normal
Grade 1
Grade 2
Grade 3
a
b
c
d
RK
RK
RK
RK
e
f
g
h
IVC
IVC
IVC
IVC
Mild
Moderate
Severe
Normal
Progression of NAFLD

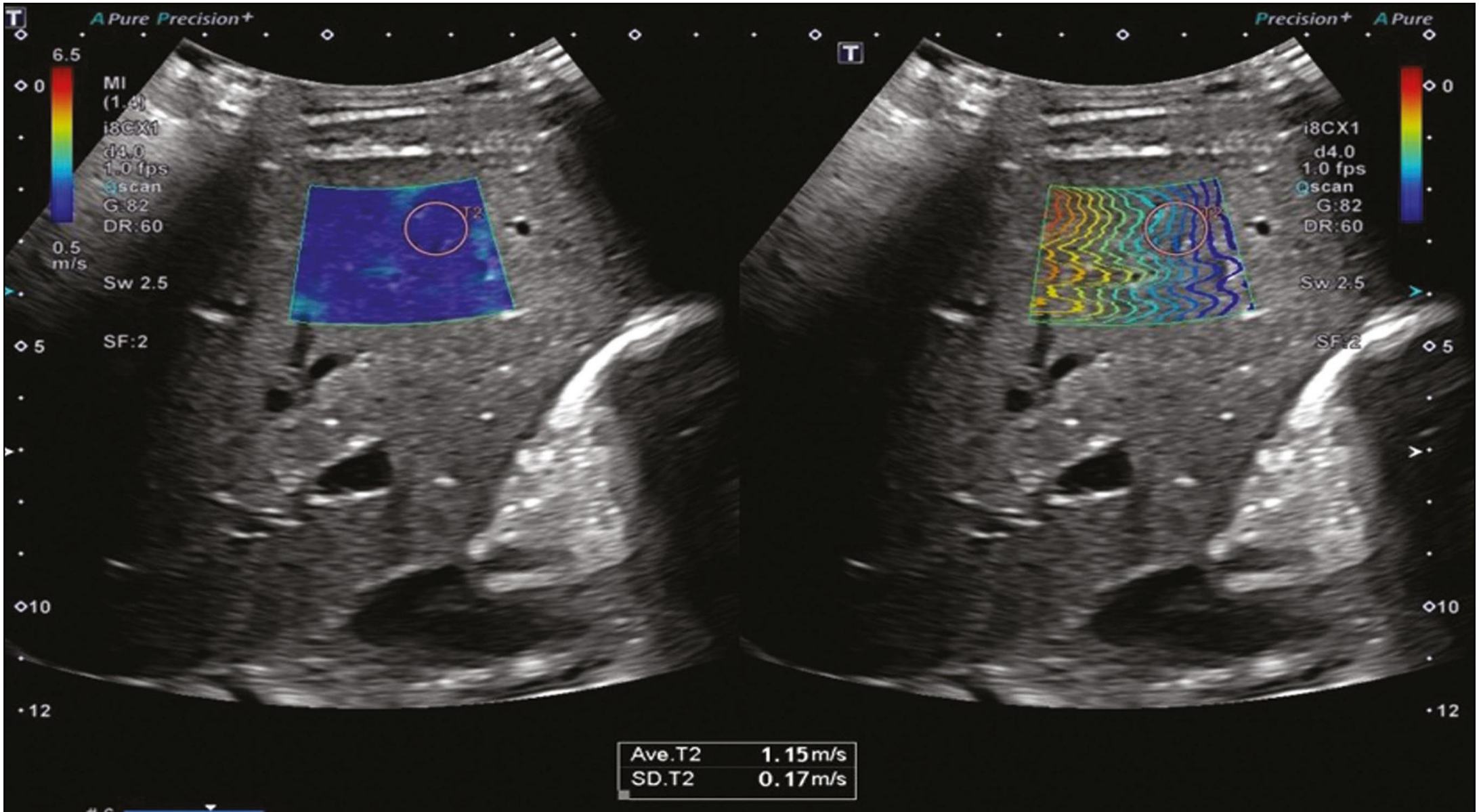
Focal fatty liver




L
K
Liver 63.59
Kidney 67.74
HRI(L/K) 0.94
L
K
Liver 88.65
Kidney 20.47
HRI(L/K) 4.33

(a) (b)

- FIBROSCAN – TRANSIENT ELASTOGRAPHY
- It is done to detect fibrosis
- A low amplitude wave is used that propagates through the liver parenchyma.
- A low liver stiffness score excludes cirrhosis.
- MRE- MAGNETIC RESONSNCE ELASTOGRAPHY
- It combines MRI with elastography and is more accurate in staging NAFLD fibrosis.
- It has sensitivity of 86% and specificity of 85% and is better than FIBROSCAN.

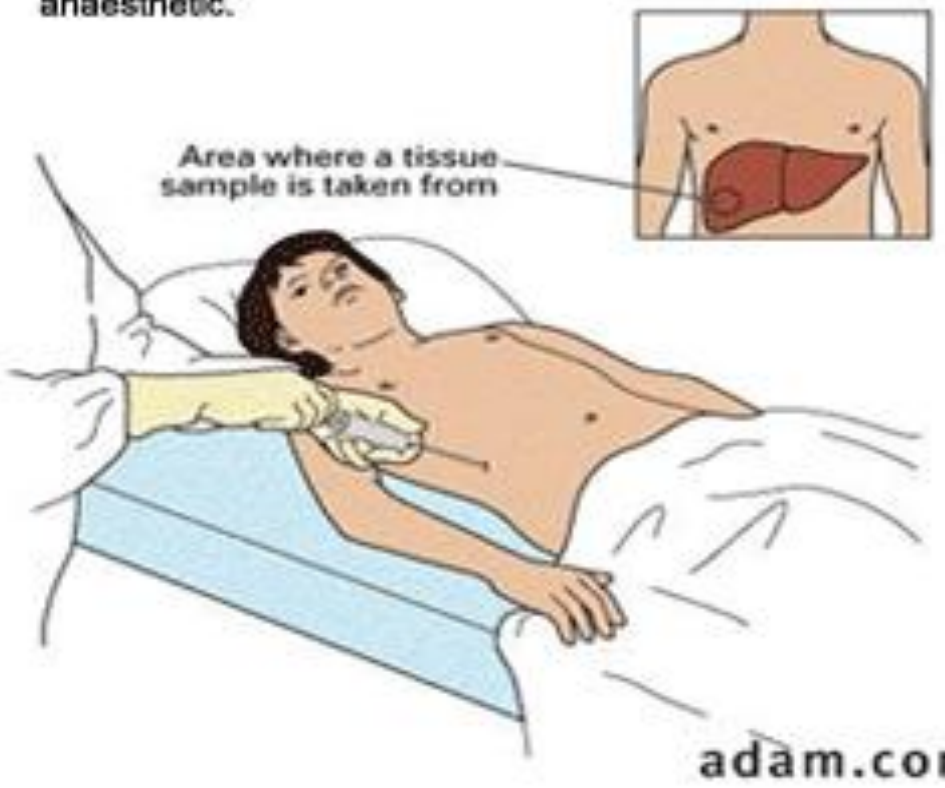

A Pure Precision+
6.5
0
MI
(1.4)
i8CX1
d4.0
1.0 fps
scan
G:82
DR:60
0.5
m/s
Sw 2.5
SF:2
5
10
12
T2
Precision+ A Pure
i8CX1
d4.0
1.0 fps
scan
G:82
DR:60
Sw 2.5
SF:2
Ave.T2 1.15m/s
SD.T2 0.17m/s

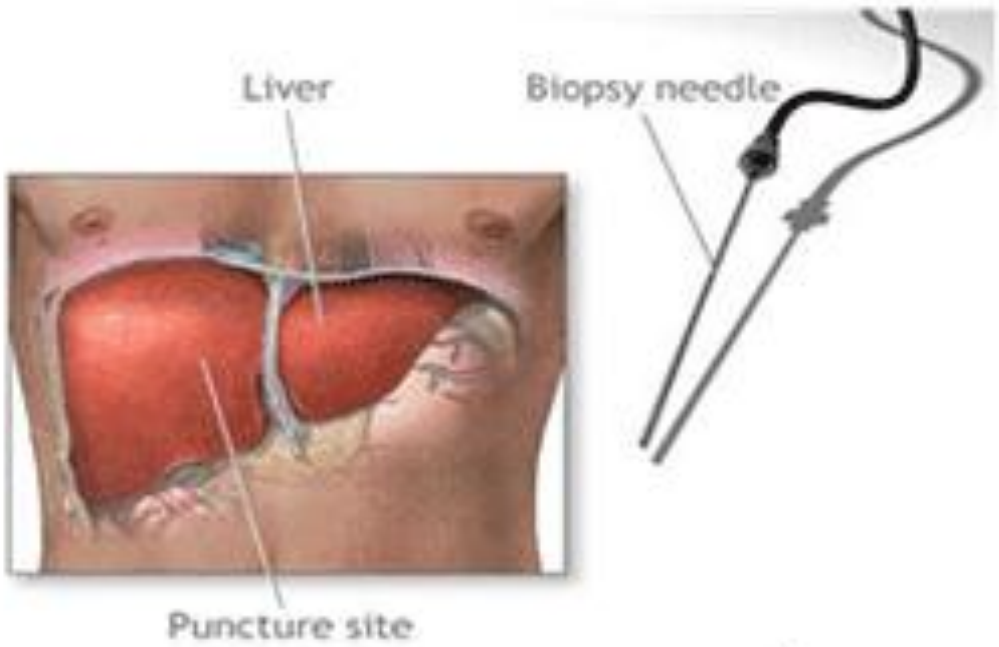
BIOPSY

- It is the gold standard for diagnosing NAFLD and establishing severity of liver injury and fibrosis.
- It is an invasive procedure with some serious but rare complications.
- INDICATIONS
- In patients with unclear diagnosis
- Persistently elevated ALT and AST levels.
- When non invasive tests suggest significant fibrosis(>F2),
- When additional/alternate diagnosis is suspected.

Liver biopsy

A tiny incision is made between the ribs and a needle is inserted in order to reach the area of the liver where a tissue sample is taken. The procedure requires a local anaesthetic.



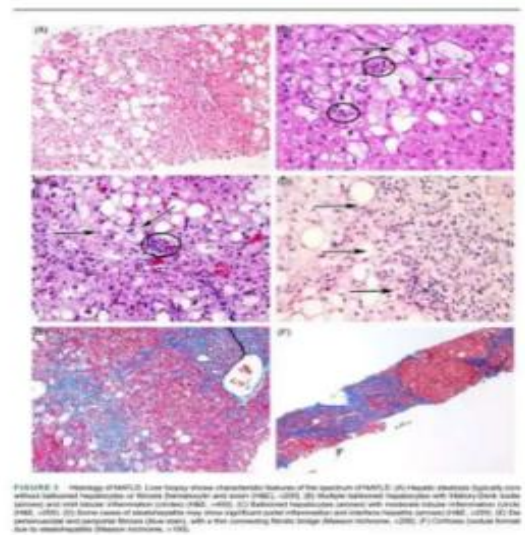


- COMPLICATIONS include hemorrhage, pain, puncture of adjacent abdominal organs biliary leak, bile stasis etc..

- LIMITATIONS
- Tissue sampling errors can be seen unless tissue cores of 2cm or more are taken.
- Examining at single point does not determine whether disease is progressing or regressing.

HISTOLOGY OF NAFLD

- A) hepatic steatosis
- B) multiple ballooned hepatocytes with Mallory hyaline bodies with mild lobular inflammation
- C) ballooned hepatocytes with moderate lobular inflammation.
- D)interface hepatitis
- E) periportal and perisinusoidal fibrosis.
- F)cirrhosis



The FIB-4 score

- is a non-invasive, widely used index—calculated using age, AST, ALT, and platelet count—to estimate liver scarring (fibrosis) in patients with liver disease like NAFLD/MAFLD.

- Interpretation of FIB-4 Scores
- Low Risk (FIB-4 <1.3 or 1.45): High probability of no advanced fibrosis, suggesting a low chance of cirrhosis.
- Intermediate Risk (FIB-4 1.3/1.45 – 3.25): Further testing (e.g., FIB-4 or FibroScan) is often recommended to clarify risk.
- High Risk (FIB-4 >2.67 or 3.25): Higher probability of advanced fibrosis/cirrhosis; warrants referral to a specialist

MANAGEMENT

- DIET AND EXERCISE
- PHARMACOTHERAPY
- DIABETES MANAGEMENT
- HYPERTENSION MANAGEMENT
- DYSLIPIDEMIA MANAGEMENT
- BERIATRIC SURGERY
- LIVER TRANSPLANTATION.

DIET AND EXERCISE

- Reduce sedentary lifestyle and increase physical activity
- Promote weight loss – 3-5% weight loss improves steatosis
- >7-10% weight loss over 6 months promotes steatohepatitis and fibrosis.
- Increase pufa, omega 3 fatty acids intake and reduce saturated fatty acids.
- Mediterranean diet has role in NASH and liver fibrosis independent of weight loss.
- Coffee intake has shown to be beneficial in reducing risk of fibrosis.
- Avoid alcohol intake.

- Exercise improves steatosis as well as insulin sensitivity
- Aerobic exercise – moderate activity for 30-60 mins for 3-5 days/ week
- Intense activity for 20-30 minutes for 2-3 days/week.
- OBESITY treatment by phentermine, orlistat, topiramate GLP -1 receptor agonists can be considered for weight control although there use is not yet approved for NAFLD management.

Diabetic Management in NAFLD

- Pioglitazone: Recommended for patients with T2DM and biopsy-proven NASH, as it improves histology and decreases liver inflammation.
- GLP-1 Receptor Agonists (e.g., Liraglutide, Semaglutide): Effective in reducing liver fat, improving liver enzymes (ALT), and aiding weight reduction.
- SGLT-2 Inhibitors (e.g., Empagliflozin, Dapagliflozin): Emerging evidence shows benefit in reducing liver fat and improving NASH, with added cardiovascular and renal protection.
- Metformin: Although widely used for T2DM, it does not directly improve liver fibrosis or histology in NAFLD.

- ANTIOXIDANTS
- VITAMIN E at a dose of 800mg/day has been accepted for use in NASH patients.
- DOC in patients without diabetes.
- PIVENS Study done showed improvement in liver enzymes, hepatic steatosis, and histology of NASH in 43% of patients treated with VITAMIN E compared to 34% in pioglitazone group and 19% in placebo group.
- TONIC trial – vit E also improved liver histology in pediatric patients with NASH.
- ADVERSE effects – hemorrhagic stroke, cardiovascular mortality, prostate cancer in patients treated for long duration.

DYSLIPIDEMIA MANAGEMENT

- Statins are first line drugs to treat dyslipidemias and to reduce cardiovascular risk.
- Use moderate to high grade statins as initial therapy.
- Statins should be avoided in decompensated cirrhosis.
- If LDL levels are not under desired range add 2nd line agents like PCSK9 Inhibitors like alirocumab, evolocumab.
- Fibrates to be used in case of increased triglyceride levels.

BERIATRIC SURGERY

- INDICATIONS
- In NASH patients with BMI> 35.
- In patients with well compensated chronic liver disease.

- CONTRAINDICATIONS
- In patients with NAFLD – CIRRHOSIS.
- CLD with portal hypertension.

LIVER TRANSPLANTATION

- NAFLD patients with end stage liver disease can be considered for liver transplantation
- It is 3rd most common cause for liver transplantation after cirrhosis caused by HCV and alcoholic liver disease.
- Outcomes are good in patients with no comorbid conditions.
- Hepatic steatosis in donor grafts is common and are associated with primary graft non function and poor overall outcomes.
- Grafts with less than 30% steatosis are acceptable for use and grafts with more than 60% steatosis are not acceptable.
- NAFLD may recur after transplantation.
- The risk factors for recurrent or de novo NAFLD after liver transplantation are multifactorial and include cardiometabolic risk factors and immunosuppressive therapies particularly steroids.

Hepatitis

- Hepatitis can be defined as inflammation of the liver cells or cells lining the biliary tract.
- It is characterized by both inflammation and necrosis of liver tissue and may be due to variety of reasons.
- This can be either acute or chronic. Some forms of hepatitis leads to rapid death, some progress to cirrhosis, while others continue as a low grade inflammation.

Types of hepatitis

TABLE 25-1 Features of Hepatitis Viruses

Hepatitis Virus	% of Viral Cases	Major Mode of Transmission	Chronic Disease Rate (% of cases)	Vaccination Available
A	48%	Fecal-oral	None	Yes
B	34%	Bloodborne; sexual transmission	<10% of adults >90% of infants	Yes
C	15%	Bloodborne	80–90%	No

Symptoms of hepatitis

- Both mild and chronic cases of hepatitis are often asymptomatic.
- The onset of acute hepatitis may be accompanied by
- Fatigue
- nausea
- Anorexia
- pain in the liver area.
- The liver is often slightly enlarged.
- **Jaundice** (yellow pigmentation of tissues) can develop, causing discoloration of the skin, urine, and the whites of the eyes.
- Other symptoms of hepatitis may include fever, diarrhea, muscle pain, and skin rashes.
- Serum levels of the aminotransferase enzymes (ALT and AST) are typically elevated.

MNT of hepatitis

- **PRINCIPLES OF TREATMENT**
- Rest
- Abstinence from alcohol
- Diet
- **Rest**
  Rest in bed is essential during the acute stage of the disease.
  The rest should be continued until:
- The appetite has returned to normal
- The liver is no longer tender
- The urine is free of bilirubin
- Normal colour has returned to the stools And serum bilirubin is less than 1.5 mg/10 ml.
- This usually involves two to three weeks of bed rest

Dietary Management

High calorie, high protein moderate fat, diet is prescribed.

Calories

3000 – 4000 K. cal/day.

A high carbohydrate diet is essential not only as a source of calories, but because of the protein value of carbohydrate in the prevention and treatment of injury to liver cells.

Protein

1.5 – 2 gs perday/kg body weight.

Ample intake of protein is essential for regeneration of liver cells.

- **Fat**
- Restrict fat if not tolerated.
- When nausea and lack of appetite are present, fat and fatty foods are poorly tolerated.
- The absorption of fat from the intestine is impaired because of lack of bile salt.
- Fried foods are badly tolerated
- The foods likely to cause dyspepsia should be avoided.

Food which cause dyspepsia

- Alcohol, strong tea, coffee, gravies and soups made from meat extracts.
- Raw vegetables, cucumber, onion, radish, tomatoes.
- Raw unripe fruit, dried fruits nuts, skins and peels of all fruits whether cooked or in puddings, cakes jams.
- Pickles, spices and condiments.
- Tough, twice cooked or highly seasoned meats including sausages, bacon and pork.

CIRRHOSIS

- Cirrhosis is an end-stage condition that results from long-term live disease.
- Liver disease gradually destroys liver tissue, leading to scarring (fibrosis) in some regions and small areas of regenerated, healthy tissue in others.
- As the disease continues, the scarring becomes more extensive, leaving fewer areas of healthy tissue.
- A cirrhotic liver is often shrunken in size and has an irregular, nodular appearance

Causes of cirrhosis

TABLE 25-2 Causes of Cirrhosis

- Alcoholic liver disease
- Autoimmune hepatitis
- Bile duct obstructions (biliary cirrhosis)
  - Diseases that cause bile duct injury
  - Complications of gallbladder surgery
  - Cystic fibrosis
- Drug-induced liver injury
- Inherited disorders
  - Hemochromatosis (causes excessive liver iron)
  - Wilson's disease (causes excessive liver copper)
  - Galactosemia
  - Glycogen storage disease
- Nonalcoholic steatohepatitis (fatty liver disease)
- Viral hepatitis (primarily hepatitis B and C)

Normal liver tissue is smooth and has a regular texture.

A cirrhotic liver has an irregular, nodular appearance. The nodules that develop in cirrhosis represent clusters of regenerating cells within the damaged liver tissue.

Lab test for evaluation of liver disease

Laboratory Test	Normal Ranges (serum)	Values in Liver Disease
Alanine aminotransferase (ALT)	Male: 10–40 U/L Female: 7–35 U/L	Elevated
Albumin	3.4–4.8 g/dL	Decreased
Alkaline phosphatase	25–100 U/L	Normal or elevated
Ammonia	15–45 µg N/dL	Elevated
Aspartate aminotransferase (AST)	10–30 U/L	Elevated
Bilirubin (total)	0.3–1.2 mg/dL	Elevated
Blood urea nitrogen (BUN)	6–20 mg/dL	Normal or decreased
Prothrombin time[a]	10–13 seconds	Prolonged

[a]The test for prothrombin time evaluates the clotting ability of blood.

Dietary guidelines of liver cirrhosis

Energy	• Without malnutrition, infection, or ascites, energy needs may (20% above basal energy expenditure (BEE); : • With malnutrition, infection, or ascites, energy needs may ran from 50% to 75% above BEE.
Protein	• Provide 1.2 to 1.5 grams protein per kilogram body weight per day to maintain nitrogen balance and prevent wasting.
Carbohydrate	• No carbohydrate restrictions. • For persons with insulin resistance or diabetes, provide up to 50% to 60% of kcalories from carbohydrates (primarily complex carbohydrates); intake of carbohydrates should be consistent from day to day and at each meal and snack.
Fat	• No fat restrictions unless fat malabsorption is present. • If fat is malabsorbed, restrict fat as necessary to control steatorrhea ; use medium-chain triglycerides (MCT) to increase kcalories.
Sodium	• Restrict sodium as necessary to control ascites; 2 to 3 grams sodium per day is adequate restriction in most cases.
Vitamins and minerals	• Ensure adequate intake from diet or supplements based on individual needs.

- **Protein**

  1.0 – 1.5 gs protein/kg/day.
  Food divided into 4–6 meals significantly improved nitrogen balance than food divided into three meals
  only.
  Vegetable proteins and milk proteins are preferred but not meat proteins.
  Vegetable proteins contain fewer AAA than meat proteins.
  Milk has the added advantage of providing both calcium, vitamin A, D and riboflavin.

  Manipulation of Amino acid ratio

  Dietary enrichment with BCAA improves nutritional status as well as neurologic dysfunction.
  Hypertonic dextose solution with 14–23% BCAA can be used with step wise increase until 37–50%
  BCAA is reached.

- **Energy**

  High kilocalorie diet (50 K. cal/Kg body weight) is recommended.

  Carbohydrate

  Adequate carbohydrate *i.e.*, 300–400 gs should be provided to spare protein.

  Excess carbohydrate may contribute to fatty liver.

  Fat

  Low to moderate fat (25% of K. cal) have to be provided if bile is inadequate

  This should be in the form of 75% medium chain triglycerides which are better utilized in liver failure

- **Sodium**

  If edema and ascites is present 500 mg sodium diet is prescribed.

  Vitamins and minerals

  Fat soluble vitamins and thiamine need to be supplemented.

  Avoid iron supplements.

  In liver disorders, copper excess is the problem.

  Increase zinc intake.

  Increased zinc intake will result in reduction in copper absorption and increases fecal copper excretion.

Dietary deficiency

Thiamine

Folic acid

Pyridoxine

Fat soluble vitamins A, K and E.

Food should be avoided in liver disease

- Sugar and unrefined carbohydrates
  - Soda, many fruit drinks, and sweetened energy drinks and teas
  - Most bakery goods such as pastries, donuts, cookies, white bread, white pasta
- Trans-fats, saturated fats, and high-fat foods
  - Fried foods
  - Butter, cream, and full-fat cheese
  - Bacon, beef, ham, lamb, sausage, organ meats
  - Trans fats are being phased out, but check ingredients for partially hydrogenated oil in foods such as microwave popcorn, frozen desserts, crackers, and stick margarine
- Sodium
  - Processed food, frozen foods, canned foods, and deli-meats
  - Snack foods with empty calories (potato chips, candy, etc.)

Food should be consumed in liver disease

- Eat vegetables — lots of them and in as many colors as possible
- Consume fruit and whole grains in moderate amounts.
- Eat plant-based or lean protein choices, such as egg whites, nonfat yogurt or milk, beans, nuts, fish and poultry.
- Choose healthy fats, such as canola and olive oil.
- Eat a fiber-rich diet.
- Reduce sodium intake. Avoid processed foods, which are often high in sodium and other additives.