NAFLD »

- Global prevelance : 20-30% of adults / up to 10% of children (due to obesity & junkfood)
- 2nd cause for liver transplant. → 3rd cause of hepatocellular carcinoma

Incidence is rising with ↑ rates of obesity, DM, physical inactivity.

Present in 7% of normal weight (lean)

Hepatic manifestation of metabolic syndrom [3 out of 5] :

① ↑ waist circumfrance ≥ 102 cm (40 in) ♂ , ≥ 88 cm (35 in) ♀

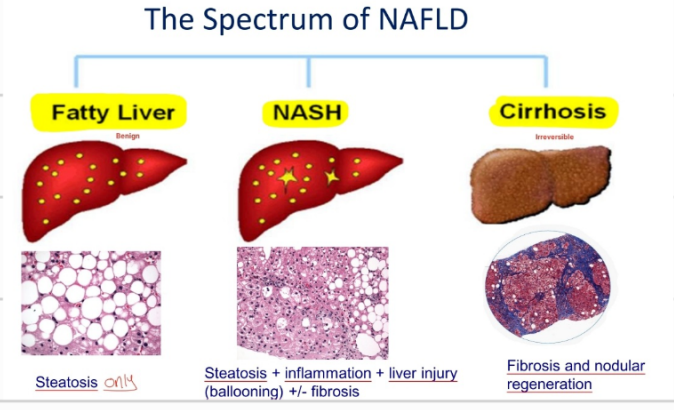
② ↑ TG ≥ 150 mg/dl

③ ↓ HDL < 40 mg/dl ♂ , <50 mg/dl ♀

④ ↑ BP ≥ 130/85 mmHg

⑤ ↑ Fasting plasma glucose ≥ 110 mg/dl (impared intolerance)

** Note: FPG > 126 criteria of DM.



- Subtypes of NAFLD: NAFL (non-progressive) ↓ 10-30% NASH (progressive)

- Pathogenesis »

•• Multi-hit hypothesis: First hits is the accumulation of fatty acids in the hepatocytes > this affects the mitochondria causing oxidative stress > increased ROS > inflammation (Kupffer cells activation) > this activates stellate cells > produces more collagen > fibrosis.

- Risk of death in NASH

-CVD -Cancer -liver

- Risk factors of progression NAFLD →

Metabolic syndrome + advance age

- prevelance 20-30% → 3-12% develop NASH → 40-50% progress to fibrosis → 15-20% cirrhosis

2-3% HCC ← → 30-40% liver death

ALT not reliable indicator for disease severity

cirrhosis develops in 20% of NASH pts.

▶ Diagnosis of NAFLD: [1] presentation
- Asymptomatic (45 – 100%)
- Minimal / non specific → fatigue, RUQ discomfort
- hepatomegaly

often "incidental" finding
↑ aminotransferase — radiographic — PE = hepatomegaly

[2] Tests
- liver tests
- Non-invasive marker
- Imaging
- Liver Biopsy

Biochemical findings:-
- AST & ALT (↑ 2-5 fold)
- AST / ALT (< 1)
- Alkaline phosphatase (↑ 2-3 fold)
- Albumin / bilirubin / INR (normal)
- Serum ferritin ↑

With all liver diseases AST\ALT ratio is <1 then with disease progression and fibrosis the ratio will be reversed bcz AST levels become higher than ALT which is a bad prognostic indicator
>> except in alcoholic liver disease the ratio is reversed from the beginning (AST\ALT is > 1)

Imaging
- US » ↑ echogenicity + Hepatomegaly
- CT » low attenuation (darker)
- Transient elastography = Fibroscan

Liver Biopsy
- gold standard
  - severity of steatosis
  - diff. simple from NASH
  - staging fibrosis

=> NASH criteria
1. steatosis > 5%
2. Mixed lobular inf
3. ballooning

fibrosis assessing
- NAFLD Fibrosis score
- FIB-4 score

Depending on parameters: Age, ALT, AST, platelet count, BMI, Albumin, FPG
- → FIB-4
- → NAFLD

>> Indication for biopsy :

1. More features of metabolic syndrome
   - Obesity, hypertension, increased TG, low HDL, impaired glucose tolerance
2. Diabetes
   - Family history of diabetes
3. Older age
4. High AST/ALT
5. Low platelets/albumin

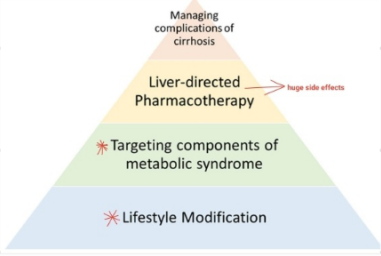
(4 and 5 indicate cirrhosis)

[3] Evaluation of suspected NAFLD

1. Exclude significant alcohol consumption
2. Exclude Secondary causes of fatty liver
3. Exclude other liver diseases
4. Imaging
5. liver biopsy

- Drugs: steroids, amiodarone, MTX, CCB, tamoxifen (estrogen receptor antagonist)
- Altered nutritional states: intestinal bypass surgery, rapid weight loss, TPN (Total parenteral nutrition), cachexia (starvation)
- Metabolic/genetic: Wilson's disease, lipodystrophy
  - Young patients who presented with fatty liver, especially in those with family history of liver diseases, perform ceruloplasmin for them as their fatty liver maybe be due to Wilson's disease
- Miscellaneous: HIV, IBD, bacterial overgrowth

- HBV, HCV (genotype 3)
- Alpha-1 antitrypsin deficiency
- Hemochromatosis (iron studies)
- Autoimmune hepatitis (ANA, ASMA)
- Wilson disease (ceruloplasmin)



[4] Managment → Aggressive manage of CV risk Factors =
→ Treat NASH

[5] Treatment

7-10% within 6-12 months ⇐ - wt. loss (most imp.)

- Diet (restrict carbs/Atkins or Mediterranean diet
  - ⊗ fructose / coffee 2-4 cups/d)
    - ↓HCC / ↓DM risk
- exercise

▶ Pharmacotherapy »

* Pioglitazone < Improve liver ✓
  wt. gain / bladder CA / Bone loss in ♀ ✗
* Vit E 800 IU/d
  - ↑risk of bleeding
  - ↑risk prostate cancer
  - ↑risk of hemorrhagic stroke
* Bariatric surgery
  - Treatment for obesity BMI > 40
  - Improve insulin sensitivity
  - ↓ steatosis, necroinflammation, fibrosis.

xx with pt. portal HTN & GE varices.

ARLD »

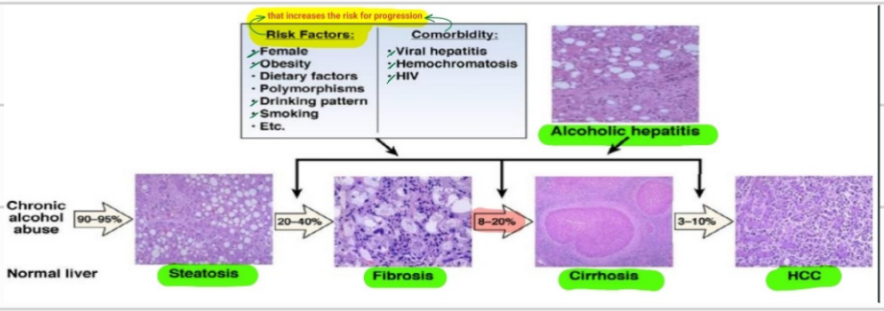
* low risk drinking → ♀ : no more than 3 drinks on any day & no more 7 drinks per week.
→ ♂ : no more 4 drinks on any day & no more 14 drinks per week

* To get alcohol related disease ⇒ Heavy alcohol 3/d ♀ (≥40g), 4/d ♂ (≥50-60 g)

3% of alcholic hepatitis progress to cirrhosis annually.

>120 g/day highest risk of cirrhosis.

*



* Out patient managment :-

1. Diff. NA from A.

2. Diagnosis alcohol use disorder

3. Managmt ⇒ Prednisolone
40mg/day
for 28 day.

*

- Remember that one cause of macrocytic non-megaloblastic anemia is Alcohol
- High MCV, male sex, low BMI, and AST > ALT favor Alcohol as factor
- Normal MCV, female sex, obesity, ALT > AST favor NASH diagnosis

Supplig nutrition gradually
↓
To avoid Refeeding syndrom
↓Kalemia ↓phosphotemia => Arythmia & Death

* DF & MELD predict mortality
↳ >32 = 50% mortality/useful for steroid treatmat.

*

Clinical Manifestations of Alcoholic Hepatitis

- Consequences of liver failure: Jaundice, Ascites, Encephalopathy
  - Patients with sever Alcoholic hepatitis may develop portal hypertension and its symptoms before even progressing to cirrhosis
- Systemic Inflammation and sepsis: SIRS (Systemic inflammatory response syndrome — an inflammatory state affecting the whole body.), Multiple organ failure → AKI, ARDS
- Impaired hepatocyte regeneration: Propagation of liver failure
- Features of alcohol withdrawal syndrome

*