American Gastroenterology Association

NASH Call to Action

Initial Evaluation of Patients with NAFLD: Clinical and Laboratory Testing in Primary Care

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Case Study

58-year-old Hispanic male

Past Medical History
- Type 2 diabetes for 8 years
- Hypertension for 12 years
- Hyperlipidemia for 8 years
- BMI 34.6 kg/m^2

Social History
- No history of smoking
- No illicit drugs
- Drinks “a few beers” on weekends

Laboratory Analysis	
ALT = 66 U/L	AST = 49 U/L

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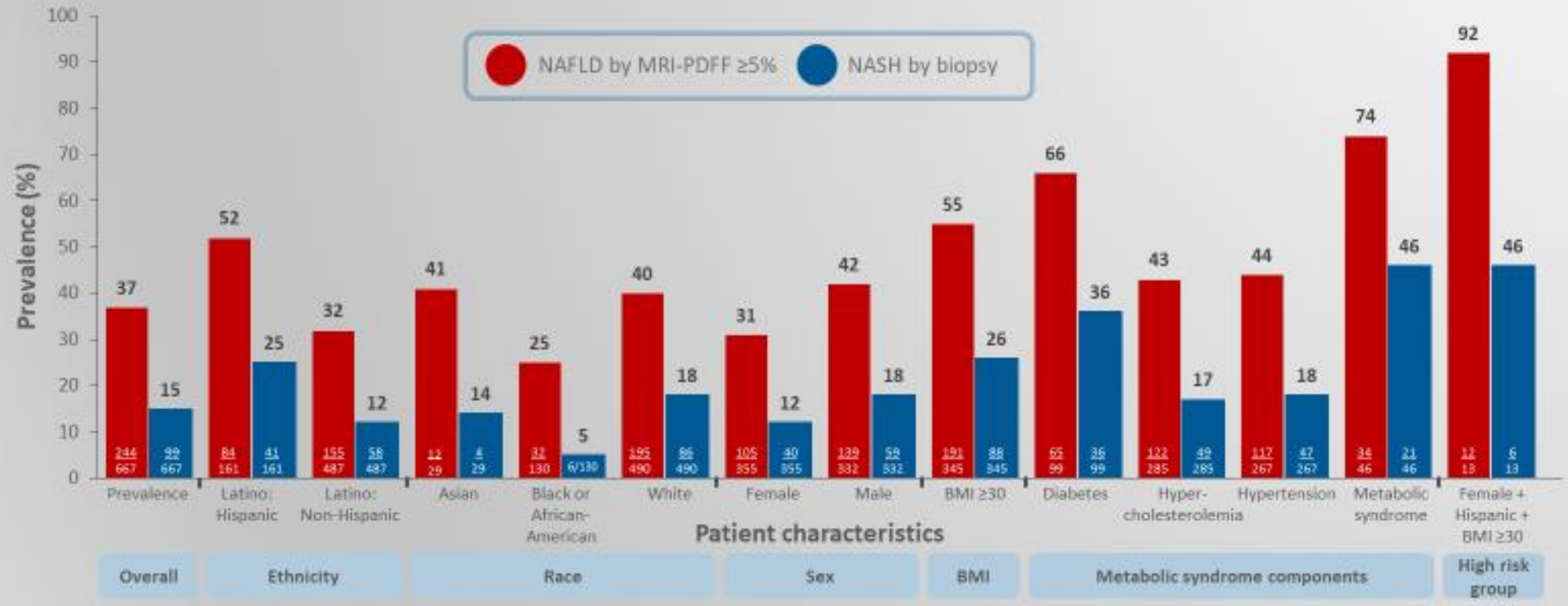
What are the patient’s risks for NAFLD/NASH?

San Antonio Prevalence Study

Results: Prevalence of NAFLD and NASH

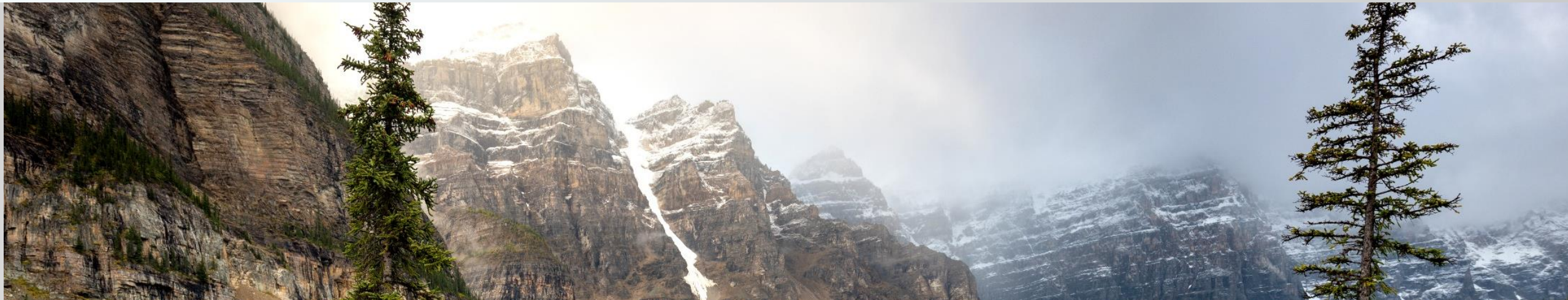
IN PATIENTS WHO RECEIVED MRI-PDFF OR BIOPSY



- BMI, body mass index; MRI-PDFF, magnetic resonance imaging – proton density fat fraction; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.

Harrison et al. EASL 2019

DIAGNOSIS



Pragmatic First Steps in Suspected NAFLD

1. Risk Identification

- Metabolic syndrome or other high prevalence group

2. History

- Alcohol intake (<14/21 units/week)
- No known pre-existing liver disease

3. Investigations

- Liver biochemistry (ALT, AST, etc)
- Exclude/identify other liver diseases:
  - Negative HBV & HCV serology
  - Negative auto-antibodies (ANA, AMA, SMA, LKM1, ANCA)
  - Negative coeliac serology
  - Normal immunoglobulins, ferritin, A1AT, Cu2+, etc.
- Liver ultrasound: increased echogenicity (steatosis)

Chalasani. Hepatology. 2018;67:328

Non-NAFLD Causes of Hepatic Steatosis

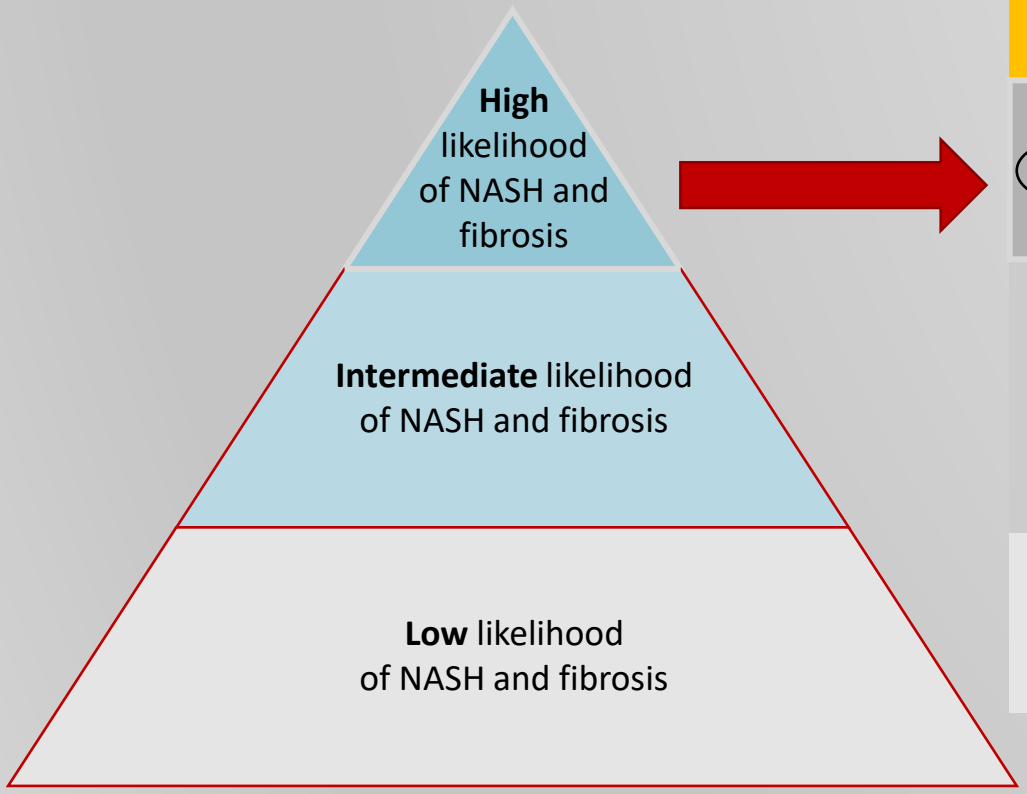
Macrovesicular steatosis:

- Significant alcohol consumption*
- Hepatitis C (genotype 3)
- Wilson's Disease
- Lipodystrophy
- Starvation
- Parenteral nutrition
- Abetalipoproteinemia
- Medications (e.g., amiodarone, methotrexate, tamoxifen, corticosteroids)

Microvesicular steatosis:

- Reye's syndrome
- Medications (valproate, antiretroviral medicines)
- Acute fatty liver of pregnancy
- HELLP syndrome
- Inborn errors of metabolism (e.g., lecithin-cholesterol acyltransferase deficiency, cholesterol ester storage disease, Wolman's disease)

Determining High Risk Features for NASH



Screening Criteria

Age, Yrs	Comorbidities	VCTE, kPA	AST, IU/L	NFS	FIB-4	Other
> 50	DM, obesity, HTN	> 8.5	> 40	> .676	> 2.67	Hispanic, AST/ALT ratio ≥ 1
> 40	Well-controlled DM, obesity, HTN	> 7.0	> 20			
< 40	No DM, no obesity	< 7.0	< 20	< -1.455	< 1.30	

Konerman. J Hepatol. 2018;68:362.

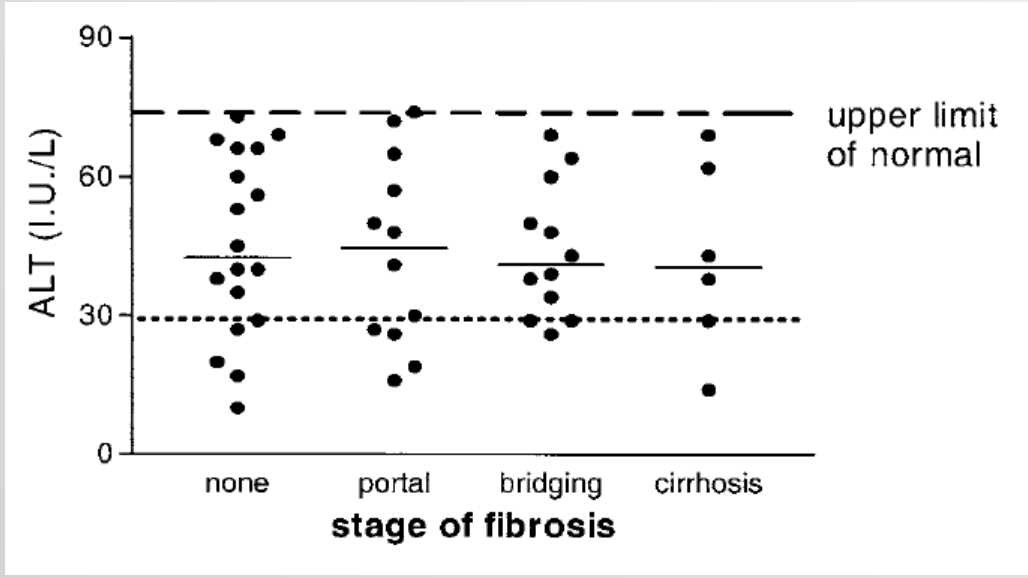
Routine Clinical Biochemistry (LFTs)

- NAFLD is the most common diagnosis in patients with 'incidental' abnormal LFTs Daniel, 1999; Skelly, 2001; Pendino, 2005

- **Liver enzymes may be normal in up to 80% of NAFLD patients** Browning, 2004
  - Transaminases are not a sensitive test for NAFLD/NASH.
  - Poor correlation between ALT and histology
  - **ALT typically falls with advanced fibrosis**
  - **ALT > AST ➔ ALT < AST**

- Severity of histology in NAFLD with normal LFTs no different from those with abnormal LFTs Mofrad, 2003; Sorrentino, 2004; Francaza, 2008

Grade/Stage of NAFLD with normal LFTs no different from those with abnormal LFTs



Mofrad et al, Hepatology 2003

Routine LFTs do not differentiate Steatosis/NASH or Stage of fibrosis

AST and Fibrosis Stage

Table 3 Comparison of clinical data between fatty liver alone and different stages of non-alcoholic steatohepatitis (NASH) fibrosis

Characteristic	Fatty liver alone	NASH stage 0	NASH stage 1–2	NASH stage 3–4	p Value
Age (years)	47 (11)	46 (11)	47 (11)	55 (11)	<0.001
Body mass index (kg/m^2)	32 (5)	33 (6)	33 (6)	35 (7)	<0.001
⩾30	77 (66%)	40 (80%)	211 (73%)	114 (79%)	
Female	62 (39%)	26 (36%)	210 (53%)	123 (63%)	<0.001
Ethnicity					
Caucasian	79 (52%)	34 (69%)	190 (70%)	92 (83%)	<0.001
African–American	17 (11%)	4 (8%)	8 (3%)	5 (4%)	
Hispanic	54 (35%)	11 (2%)	65 (24%)	12 (11%)	
Asian Pacific Islander	3 (2%)	0 (0)	8 (3%)	2 (2%)	
Hypertension	73 (47%)	41 (70%)	177 (61%)	100 (69%)	<0.001
Diabetes	23 (15%)	15 (23%)	115 (34%)	106 (60%)	<0.001
Alanine aminotransferase (ALT) (U/l)	68 (37)	80 (37)	92 (72)	67 (44)	<0.001
Aspartate aminotransferase (AST) (U/l)	42 (19)	47 (20)	62 (44)	70 (45)	<0.001
AST/ALT ratio	0.7 (0.3)	0.6 (0.3)	0.8 (0.3)	1.2 (0.5)	<0.001
QUICKI	0.318 (0.029)	0.295 (0.026)	0.303 (0.030)	0.293 (0.020)	<0.001
Hyperlipidaemia					
Neg	103 (65%)	33 (51%)	179 (52%)	109 (66%)	0.002
Pos	55 (35)	32 (49%)	166 (48%)	55 (34%)	

QUICKI, quantitative assessment check index.

Harrison SA, Gut 2008

= Risk Factor

Back to Our Case Study

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