

Emerging Trend in Epidemiology of NAFLD and Long-term Outcome

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Introduction

- Nonalcoholic fatty liver disease(NAFLD) has emerged as the most prevalent liver disease worldwide, mainly because of the massive parallel global increase in obesity
- Extensive public-health and political efforts will be needed in the near future to counteract this disturbing development

- Traditionally, obesity and its related diseases have been considered a problem in Western countries
- In the past two decades, urbanisation in many Asian countries has led to a sedentary lifestyle and overnutrition, setting the stage for the epidemic of obesity

- The term NASH was coined in 1989
- After another decade, it was recognized that NASH is a part of the clinicopathologic spectrum of NAFLD

Definition

- Accumulation of fat within the liver (hepatic steatosis) with no other known cause of hepatic fat accumulation
- No evidence of excessive alcohol use
Men: 3 drinks / day Women: 2 drinks / day
- Presence of fat defined by imaging or biopsy of liver
- NAFLD can be found in non-obese individuals

- **lack of secondary causes** of hepatic fat accumulation such as significant alcohol consumption, longterm use of a steatogenic medication, or monogenic hereditary disorders
- commonly associated with metabolic comorbidities such as obesity, diabetes mellitus, and dyslipidemia

- **NAFLD** ---histologically into nonalcoholic fatty liver (NAFL) or nonalcoholic steatohepatitis
- **NAFL** ---the presence of 5% HS **without** evidence of hepatocellular injury in the form of hepatocyte ballooning
- **NASH** --- presence of 5% HS and inflammation **with** hepatocyte injury (e.g., ballooning),with or without any fibrosis
- For defining “advanced” fibrosis--referring specifically to stages 3 or 4, that is, bridging fibrosis or cirrhosis.

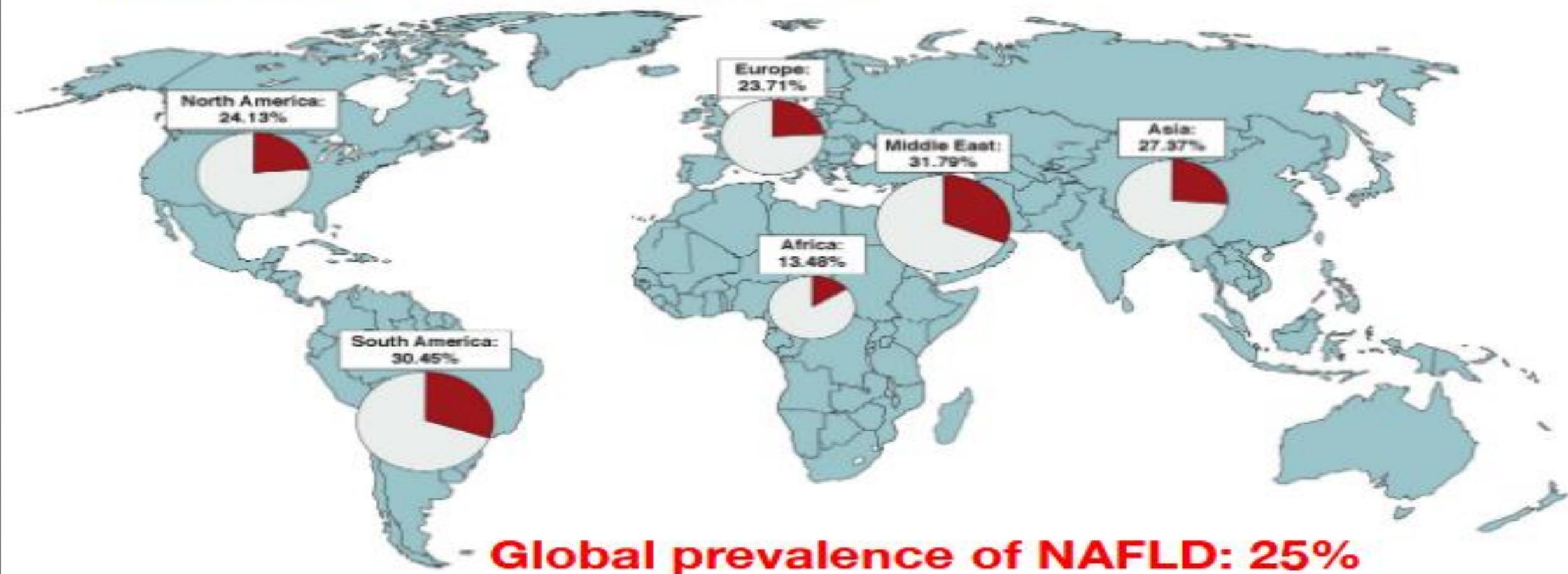
NAFLD in the West and Asia

	Western countries	Asian countries
Prevalence of NAFLD	25%	25%
Proportion of NAFLD patients with NASH	20–30%	10–20%
Proportion of NAFLD patients with F3-4 fibrosis	10%	3–5%
Prevalence of NAFLD in subjects with BMI<25	10%	7–19%

- Currently, the population prevalence of NAFLD in Asia is around 25%, like many Western countries. While hepatocellular carcinoma and end-stage liver disease secondary to NAFLD remain uncommon, a rising trend has emerged
- Around 8–19% of Asians with body mass indexes less than 25 kg/m² are also found to have NAFLD, a condition often described as “lean” or “non-obese” NAFLD
- Although this condition is generally less severe than that in more obese patients, steatohepatitis and fibrotic disease are well recognized

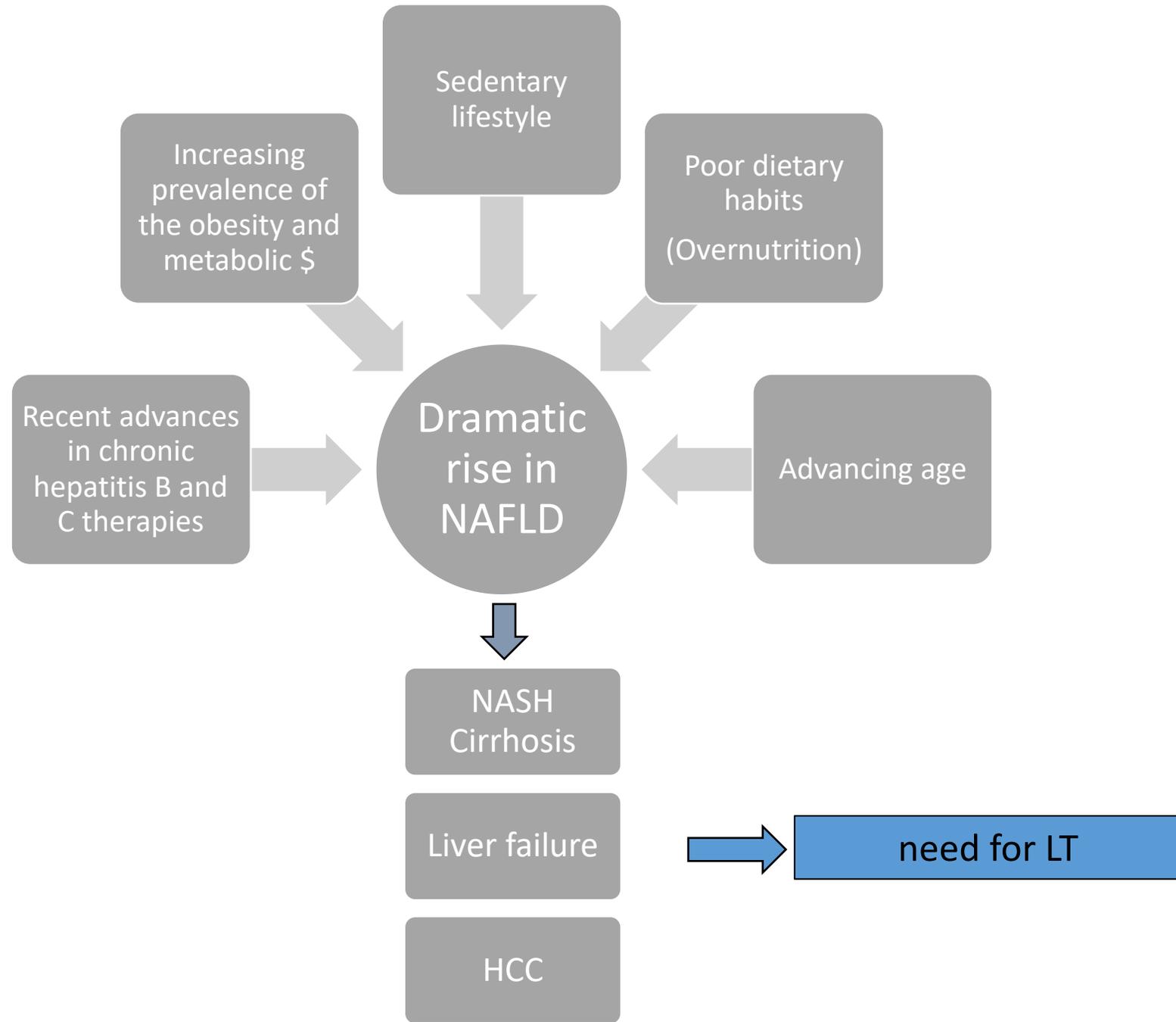
Global prevalence of NAFLD

Global prevalence of overweight and obesity: 39%



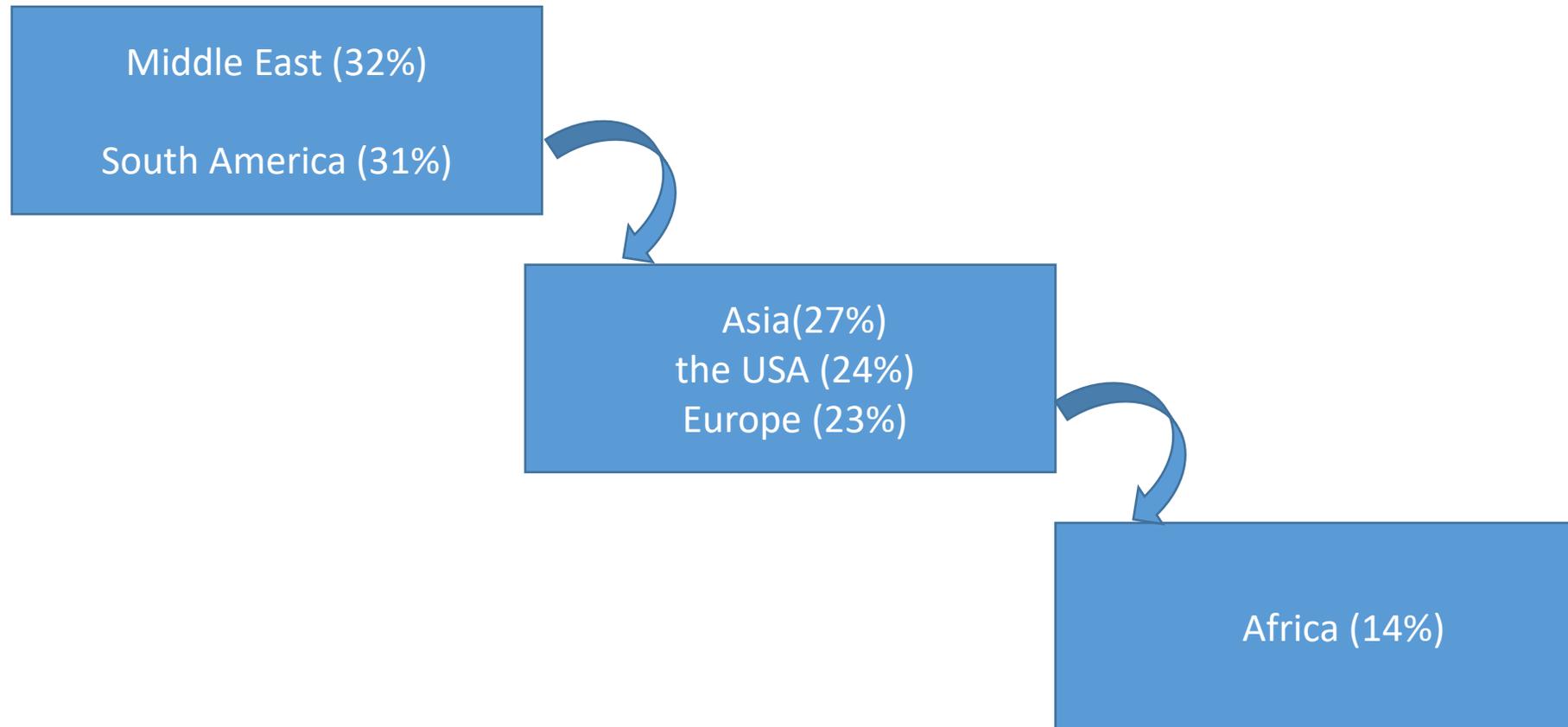
- **Central adiposity, insulin resistance and weight gain** are major risk factors, and **genetic predisposition, such as the PNPLA3 polymorphism** appears to be more important in the development of NAFLD in the non-obese population
- Lifestyle modification remains the cornerstone of management for obesity and NAFLD, but few patients can achieve adequate weight reduction and even fewer can maintain the weight in the long run

- Recent advances in chronic hepatitis B and C therapies, combined with increasing prevalence of the obesity epidemic and of other metabolic disorders, such as type 2 diabetes mellitus (T2DM) and hyperlipidemia, have led to → dramatic rise in NAFLD
- Today, NAFLD is a major global health problem and has emerged as the 2nd most common indication for liver transplantation (LT) in the USA, and is projected to become number 1 soon



- As noted previously, due to the growing obesity epidemic now affecting more than 1.9 billion adults globally
- According to recent estimates, NAFLD affects as many as one billion individuals throughout the world
- Similarly, in the USA, NAFLD affects nearly 80-100 million individuals, making it the number 1 etiology of CLD
- Nearly 25% of patients with NAFL progress to NASH; however, the true prevalence of biopsy-proven NASH is difficult to determine, as the majority of NAFL patients do not undergo biopsy
- Although the prevalence of NAFLD is increasing throughout the world, there appears to be a significant geographical variation

➤ The global prevalence of NAFLD is currently estimated to be 25%



- Due to the increased prevalence of NAFL, the prevalence of NASH is expected to increase as well
- the proportion of NAFL cases that progress to NASH will increase from **20% to 27% by 2030**
- Similarly, incident of decompensated cirrhosis is predicted to increase by **168%**, from **39,230 cases annually in 2015 to 105,430 cases in 2030**

- The prevalence of NAFLD continues to increase, and it is expected that NASH-related end-stage liver disease (ESLD) will become the leading indication for LT over the next several decades
- The corresponding burden of NASH cirrhosis on liver transplantation (LT) is expected to increase by **59%**
- Numerous recent studies have reported that NASH-related cirrhosis is the most rapidly growing indication for LT in the USA

- In 2017, Cholankeril et al., using data from the United Network for Organ Sharing and Organ Procurement and Transplantation Network (commonly known as UNOS/OPTN) database, reported a **162%** increase in **LT secondary to NASH** from **2003 to 2014**
- while LT due to alcoholic liver disease (**ALD**) and hepatitis C virus (**HCV**) only increased by **54%** and **33%** respectively
- As the burden of NASH-related ESLD on the wait-list continues to rapidly grow, the risk of wait-list removal secondary to death or progression of comorbidities increases

Long term outcome of NAFLD

Good outcome

- NASH resolution can be achieved by targeted weight loss
 - Diet
 - Physical exercise
 - Pharmacological treatment
 - Surgical intervention
- NAFLD without significant fibrosis can regress completely

Long term outcome of NAFLD

Bad outcome

- Liver related
 - NASH is the risk of
 - liver failure
 - liver fibrosis/cirrhosis
 - HCC
 - Advanced fibrosis
 - Higher age
 - Family history of HCC
 - Lower serum Albumin
 - Higher GGT
 - Insulin treatment for DM
 - Chronic viral hepatitis infection

Long term outcome of NAFLD

Bad outcome

- Non-liver related
 - CVD risks and complications (Cardiovascular diseases like MI, stroke) influenced by both (genetics) and (environment and diet)
 - Obesity related complication like Obstructive sleep apnoea syndrome
 - Increased risk of developing DM and closely related to degree of glucose intolerance
 - Hyperuricaemia, gout, chronic kidney disease, gallstone disease
 - Poly cystic ovarian \$
 - Colorectal adenomatous polyp and colorectal cancer

Summary

- Nonalcoholic fatty liver disease (NAFLD) has emerged as the most prevalent liver disease worldwide, mainly because of the massive parallel global increase in obesity
- Define--Accumulation of fat within the liver (hepatic steatosis) with no other known cause of hepatic fat accumulation
- Currently, the population prevalence of NAFLD in Asia is around 25%
- Today, NAFLD is a major global health problem and has emerged as the 2nd most common indication for liver transplantation (LT) in the USA, and is projected to become number 1 soon
- Long term outcome of NAFLD --Good outcome, Bad outcome



THANK YOU