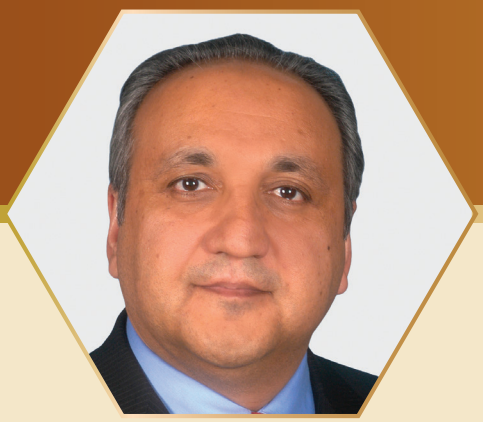
1st GLOBAL LIVER HEALTH FORUM

Insights into NAFLD burden and epidemiology– what does the data tell us? Global insights



Prof Zobair M. Younossi

President of Inova Medicine, Inova Health System and the Chairman and Professor of Medicine, Inova Fairfax Medical Campus, Virginia, USA.

Flash for webinar (~20 mins)

SANOFI

Insights into NAFLD burden and epidemiology– what does the data tell us? Global insights

Prevalence of NAFLD across different geographical regions

The prevalence of NAFLD in Europe is increasing, and currently ranges between 20-30%, depending on the country.[1–3] The overall prevalence of NASH is 3%.[1] Similar increases in NAFLD prevalence are apparent across Asia: some countries e.g. Japan report a prevalence of ≥30%.[4] The growing prevalence of NAFLD in the Middle East, Africa and Latin America tracks that of increasing rates of obesity and metabolic syndrome.[5,6]

In the USA, yearly trend analyses showed that the only liver disease with consistently increasing prevalence over the past three decades was NAFLD (trend p=0.01).[7]

The burden of NAFLD: a progressive disease

NAFLD is a spectrum disease with non-linear progression.[8] Progression to NASH is associated with considerable morbidity – including cirrhosis, hepatocellular carcinoma and need for liver transplantation – and mortality.[3]

Data from the USA show that between 2007 and 2017, the increase in age-specific death rate for HCC due to ALD and NAFLD accelerated after 2014, whereas CHC stabilized.[9] Furthermore, since 2002 there has been a steady increase in the number of NASH patients +/- HCC requiring a liver transplant.[10] The future clinical burden of NAFLD/NASH is predicted to continue to rise: by 2030, it has been projected that there will be nearly 800,000 excess liver deaths.[11]

Data from the Global Burden of Disease survey (2007–2017) were used to assess years lost due to disability (YLD), years of life lost (YLL), disability-adjusted life-years (DALYs) and temporal trends (2007–2017) for 21 regions and 195 countries.[12]

In 2017, there were 62.16 million DALYs related to NAFLD (33.4% LC; 66.5% cirrhosis); these were mostly (96.8%) attributed to YLL (96.8%).13 Between 2007–2017, NAFLD showed the largest increase in DALYs.[13]

NAFLD and associated comorbidities

NAFLD is part of a multisystem disorder and is related to obesity and metabolic disorders.[14] NAFLD patients aged 40–70 years with higher Atherosclerotic Cardiovascular Disease (ASCVD) scores, indicating high risk for CVD, had much higher overall mortality (56% vs. 16.8%) than patients with low scores at low CVD risk, ASCVD score <7.5%.[15] Furthermore, physical inactivity is related to sarcopenia and to increased mortality among NAFLD patients.[16]

EPL: essential phospholipids; **NAFLD:** non-alcoholic fatty liver disease; **NASH:** non-alcoholic steatohepatitis; **HCC:** hepatocellular carcinoma; **ALD:** alcoholic liver disease; **CHC:** chronic hepatitis; **HRQoL:** health related quality of life.

Insights into NAFLD burden and epidemiology– what does the data tell us? Global insights

Although most NAFLD patients are obese, there are some patients with lean NAFLD. NAFLD was independently associated with increased risk of all-cause and cardiovascular mortality in lean individuals.[17] Visceral obesity in patients with lean BMI is associated with higher risk of NAFLD-associated mortality.[16]

Patient-reported outcomes (PRO) in NAFLD/NASH

Fatigue/tiredness (71%) and overweight (62%) are the most common patient-reported symptoms in NASH.[18] Fatigue is associated with impairment in a wide variety of other patient-reported outcomes.[18] Predictors of clinically significant fatigue scores were found, in a multivariate analysis of NASH patient data, to include neuro-psychiatric comorbidities, T2DM and some laboratory tests.[19]

Economic burden of NAFLD/NASH

Markov modelling of US costs associated with NASH, based on 6.65 million adults with NASH in the US and 688,000 cases of advanced NASH, suggests lifetime direct costs of all NASH of $222.6 billion and lifetime direct costs of advanced NASH of $95.4 billion.[20–21]

EPL: essential phospholipids; **NAFLD:** non-alcoholic fatty liver disease; **NASH:** non-alcoholic steatohepatitis; **HCC:** hepatocellular carcinoma; **ALD:** alcoholic liver disease; **CHC:** chronic hepatitis; **HRQoL:** health related quality of life.

Insights into NAFLD burden and epidemiology– what does the data tell us? Global insights

References

1. Younossi Z, *et al.* Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. Hepatology. 2019;69:2672–82.
2. Tsukanov V, *et al.* AGA 2011; Abstract Mo2025.
3. Younossi ZM. Non-alcoholic fatty liver disease - A global public health perspective. J Hepatol. 2019;70:531–44.
4. Li J, *et al.* Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999-2019: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2019 May;4(5):389-398.
5. Ahmed MH, *et al.* Non-Alcoholic Fatty Liver Disease in Africa and Middle East: An Attempt to Predict the Present and Future Implications on the Healthcare System. Gastroenterol Res. 2017;10:271–9.
6. López-Velázquez JA, *et al.* The prevalence of nonalcoholic fatty liver disease in the Americas. Ann Hepatol 2014;13:166–78.
7. Younossi Z, *et al.* Epidemiology of chronic liver diseases in the USA in the past three decades. Gut. 2020;69:564–8.
8. Younossi Z, *et al.* Diagnostic modalities for nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, and associated fibrosis. Hepatology 2018;68:349–60.
9. Paik JM, *et al.* Nonalcoholic Fatty Liver Disease and Alcoholic Liver Disease are Major Drivers of Liver Mortality in the United States. Hepatology Communication. 2020;4:890–9.
10. Younossi ZM, *et al.* Nonalcoholic Steatohepatitis Is the Fastest Growing Cause of Hepatocellular Carcinoma in Liver Transplant Candidates. Clin Gastro Hepatol. 2019;17:748–55.
11. Estes C, *et al.* Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. Hepatology. 2018;67:123–133.
12. GBD 2017 DIIPC. Lancet. 2018 Nov 10;392:1789-1858.
13. Paike JM, *et al.* J Hepatol 2020;73:S19–S57. Abstract AS063.
14. Byrne CD & Targher G. NAFLD: a multisystem disease. J Hepatol. 2015;S47–S64.
15. Golabi P, *et al.* Mortality Risk Detected by Atherosclerotic Cardiovascular Disease Score in Patients With Nonalcoholic Fatty Liver Disease. Hepatology Communications. 2019;31050–60.
16. Golabi P, *et al.* Mortality of NAFLD According to the Body Composition and Presence of Metabolic Abnormalities. Hepatology Communications. 2020;4:1136–48.
17. Golabi P, *et al.* Patients with lean nonalcoholic fatty liver disease are metabolically abnormal and have a higher risk for mortality. Clinical Diabetes. 2019;37:65-72.
18. Cook N, *et al.* The Patient Perspectives on Future Therapeutic Options in NASH and Patient Needs. Frontier in Medicine. 2019;6:61.
19. Younossi ZM, *et al.* Reduced Patient-Reported Outcome Scores Associate With Level of Fibrosis in Patients With Nonalcoholic Steatohepatitis. Clin Gastro Hepatol. 2019;17:2552–60.
20. Younossi ZM, *et al.* The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. Hepatology. 2016;64:1577–86.
21. Younossi ZM, *et al.* Burden of Illness and Economic Model for Patients With Nonalcoholic Steatohepatitis in the United States. Hepatology. 2019;69:564–72.

Insights into NAFLD burden and epidemiology– what does the data tell us? Global insights

Learning objectives:

The prevalence of NAFLD and NASH is increasing worldwide, with specific country and regional differences.

NAFLD is creating an extraordinary burden of clinical, economic and QoL-related factors.

Recognition of the comorbidities associated with NAFLD and their potential impact on NAFLD outcomes is key.

Main take aways:

NAFLD/NASH are part of a multisystemic disease related to metabolic abnormalities.

NAFLD and NASH have a significant and growing clinical, economic and quality of life burden.

NASH is common and potentially progressive type of NAFLD.

NAFLD/NASH are rapidly becoming the most common cause of cirrhosis, hepatocellular carcinoma and indication for liver transplantation in the world.

1st GLOBAL LIVER HEALTH FORUM

SANOFI

MAT-GLB-2003464