Nonalcoholic Fatty Liver Disease: Disease Burden and Disease Awareness

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KEYWORDS

• Fatty liver • Epidemiology • Prevalence • Disease burden • Awareness

KEY POINTS

- The global prevalence of NAFLD has been increasing for the last two decades.
- South America, Middle East and Asia have the highest prevalence of NAFLD while some regions in Africa have reported the lowest prevalence.
- Among NAFLD, the proportion of patients with NASH is increasing as well, which will, in turn, increase the number of patients with advanced liver disease in the coming years.
- The disease awareness in both the patients and providers is suboptimal.Even though primary care settings could represent the first level of encounter for patients with undiagnosed NASH and provide an opportunity for risk stratification, very few programs are being implemented in clinical practice.
- Considering the worsening burden of NAFLD and related adverse outcomes, more needs to be done to increase disease awareness across different stakeholder groups.

INTRODUCTION

After four decades since the term nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver disease (NAFLD), there is growing evidence to suggest that they are rapidly becoming the most common causes of liver disease across the world.[1]

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Clin Liver Dis 27 (2023) 173–186
https://doi.org/10.1016/j.cld.2023.01.001 **liver.theclinics.com**

As the name implies, fatty infiltration of hepatocytes in the absence of secondary causes, including excessive alcohol consumption, is the cornerstone of NAFLD. It encompasses a spectrum of liver pathology, ranging from simple steatosis to NASH, which is regarded as the more progressive form of NAFLD.[2] It has been shown that some patients with NASH develop hepatic fibrosis leading to cirrhosis and hepatocellular carcinoma.[3–7]

NAFLD has become a highly prevalent, alarming health care providers and policy makers across the globe in the last decades. NAFLD prevalence has been increasing at an unprecedented rate, with an estimated global prevalence rate ranging between 24% and 38%.[1,4,8,9] It is also estimated that up to 20% of patients with NAFLD may have underlying NASH.[10] Understandably, those rates are even higher among patients with type 2 diabetes (T2DM), obesity, and especially those undergoing bariatric surgery (see chapter 16).[11] However, NAFLD prevalence is not uniform globally and demonstrates variations based on the population studied. Possible explanations for this heterogeneous prevalence rate include different rates of risk factors across different geographic regions, genetic factors, environmental factors, and cultural elements.[12]

Although NAFLD is a liver disease, it is regarded as a part of multisystemic diseases that include cardiovascular disease, extrahepatic cancers, sarcopenia, and other conditions associated with metabolic syndrome[13–15] (see chapters 2, 5-7). In fact, underlying insulin resistance seems to be the underpinning of NAFLD and other related comorbidities. It is also important to note that the presence of T2DM is an independent predictor of advanced fibrosis and mortality among NAFLD population.[16,17]

The progression of NASH seems to be nonlinear with patients following a slowly progressive course for a period of time, followed by periods of regression. Given the sheer number of patients with NAFLD and NASH, a large number of patients can present with advanced fibrosis, cirrhosis, hepatocellular carcinoma, and requirement for liver transplantation[18,19] (see chapter 3,4). In fact, after the introduction of effective treatment options for viral hepatitis in the last decade, NAFLD/NASH and alcoholic liver disease have become the main indications for liver transplantation in the United States[20,21] (see chapter 14). In addition to clinical consequences, NAFLD/NASH also causes significant economic burden as well as impairment with its patient-related outcomes. This comprehensive burden not only affects patients but also communities and the whole health care systems.

Even though NAFLD/NASH is highly prevalent and possesses an unquestionable burden to patients and health care systems (see chapter 20), treatment options are very limited (see chapter 15). In fact, lifestyle modification with diet and exercise has been cornerstone of treatment of NAFLD.[2] However, in practice, the proportion of patients who can achieve and sustain the recommended weight loss remains very small. In the last decade, there have been significant efforts to develop pharmacologic agents for the treatment of NASH and related fibrosis.[22,23] Multicenter and multinational trials are being carried out without a successfully approved pharmacologic regimen[24,25] (see chapter 17). Considering the high prevalence and progressive nature of NAFLD/NASH, it is important to identify patients who are at risk of progressive liver disease and adverse outcomes. In this context, risk stratification algorithms are being developed to identify NAFLD patients at risk for developing advanced fibrosis and cirrhosis and link these patients for specialty care such as gastroenterology and hepatology. In addition to limited treatment options, awareness about the disease is poor at primary care and other front-line provider settings. Programs to improve awareness, case finding, and linkage of those at risk will be of great importance.

In the following sections, the authors review the burden of NAFLD related to prevalence and mortality.

NONALCOHOLIC FATTY LIVER DISEASE BURDEN

As stated above, most recent reports suggest that the global prevalence of NAFLD is around 30% to 32% in the general population. More importantly, NASH prevalence has been increasing and is now estimated to be around 5.3% globally.[8–10,26] The highest prevalence rates have been reported from South America, Middle East, and Asia, whereas the lowest rates were seen in some parts of Africa.[27,28]

North America

In North America, the vast majority of data originate from the United States. Understandably, noninvasive methods, such as imaging or blood tests, were most recently used, rather than liver biopsy, which is still regarded as the gold standard for diagnosis. In the general US population, NAFLD prevalence has continued to worsen in the last decade. Even though a previous meta-analysis reported a prevalence rate of 24% in the general US population, the most recent meta-analysis suggests a pooled global prevalence rate of 31.2% from 1990-2019.[9,26] In fact, the prevalence for 2016-2019 was 38.2%.9 Nevertheless, NAFLD prevalence shows variations in different ethnic groups, and Hispanic Americans and Americans from European descent have higher NAFLD rates than African Americans.[29,30] Furthermore, even within a certain ethnic group, NAFLD prevalence shows variations based on the country of origin. It has previously been demonstrated that although NAFLD prevalence is 29% among Hispanic Americans, it is 33% among those of Mexican origin, 18% among those of Puerto Rican origin, and 16% among those of Dominican origin.[31] These rates suggest both potential genetic predisposition and environmental factors that may affect diet and activity habits. More studies are needed to better understand the ethnic differences among NAFLD patients in North America.

South America (see chapter 9)

Compared with the United States, NAFLD prevalence seems to be higher in South America, with an estimated prevalence rate of 44.4% in the general population.[9,32,33] In a multicenter study in Brazil among 1280 patients, the prevalence of NAFL, NASH, and fibrosis was 42%, 58%, and 27%, respectively.[34] Furthermore, NAFLD prevalence of 26.6% was reported among young males in Colombia, whereas the rate was 22% in Chile.[35,36] Finally, a cohort study among 2500 patients in Mexico showed a prevalence rate of 17.1%.[37] It is important to note that study design and modalities used to establish the diagnosis of NAFLD can explain some of the differences in the reported rates.

Similar to North America, the prevalence of NAFLD and NASH in these multiethnic populations is affected by different genetic factors such as single-nucleotide polymorphism of patatin-like phospholipase domain containing protein 3 (PNPLA3) as well as environmental factors affecting diet and activity.

Asia (see chapter 8)

NAFLD prevalence rates demonstrate a wide variation in Asian countries, likely due to different levels of economic development and dietary habits. Even within the same country, such as China, significant regional differences have been observed. In a recent meta-analysis, the prevalence of NAFLD was 33.9% in South Asia, 33.1% in Southeast Asia, 29.7% in East Asia, and 28% in Asia Pacific region.[9] Again, the

method of diagnosis and study design could impact these reported prevalence rates. In this context, previous studies have shown that the prevalence of NAFLD according to proton magnetic resonance spectroscopy was 19.3% in nonobese patients and 60.5% in obese individuals from Hong Kong.[38] On the other hand, in Shanghai, NAFLD diagnosis based on ultrasound reported a prevalence rate of 38.2% among 7152 individuals.[39] Even though lower rates were also reported in some rural regions of China, dietary habits and lifestyle differences seem to be responsible for these differences. Similar to China, a significant difference in the NAFLD prevalence rates was observed between rural (9%) and urban (32%) areas of India.[40,41] In Japan and Korea, NAFLD prevalence rates were found to be comparable to North America, with 26% and 27%, respectively.[42,43]

Africa and Middle East (see chapter 9)

There have been very limited epidemiologic data from Africa, making it difficult to assess the prevalence of NAFLD reliably. Nevertheless, the prevalence of NAFLD in Africa seems to follow the prevalence of obesity and T2DM. Overall, the prevalence seems to be lower. In fact, NAFLD prevalence was reported to range from 1.2% to 4.5% in Nigeria. On the other hand, 50% to 69% of diabetics in Sudan and Nigeria seem to have NAFLD.[44–47]

In contrast, the rates of NAFLD in the North African countries are similar to those reported from the Middle East. In fact, the Middle East and North Africa region has one of the highest NAFLD prevalence rates and experiences a very high burden of disease.[27] Based on the most recent meta-analytic assessments, NAFLD prevalence in this region has reached 36.5%, which is higher than previously reported rates.[4,9] At the country level, population-based reports from Iran reported that NAFLD prevalence might be as high as 39%, with urban areas being affected more heavily than rural areas.[48,49] The scenario is even worse in the neighboring country, Turkey where a recent cross-sectional study among 15 centers with more than 113,000 participants reported the prevalence of ultrasound-based NAFLD of 48.3%.[50] These rates were higher among older individuals (>50 years of age, 65.6%) and males (65%). Again, lifestyle choices and dietary habits seem to play a role in NAFLD prevalence even within the same country. In this context, the NAFLD prevalence was lower in the Aegean region of Turkey (West), where the Mediterranean diet is common as compared with Central Anatolia (39.8% vs 57.1%) and a more carbohydrate and a red meat-rich diet is common. Furthermore, this study demonstrated 22% increase in NAFLD prevalence between 2007 to and 2010 (43.5%) and 2014 to 2016 (53.1%) years.[50]

Europe

Depending on the region, NAFLD prevalence ranges between 20% and 30% across Europe in the general population level.[9] Most of the reports diagnosed NAFLD based on ultrasound data in this region. Not surprisingly, if the focus is turned into “at-risk” populations, such as those with T2DM, NAFLD prevalence rates increase substantially. A multicenter, cross-sectional, population-based study in Spain, across 25 centers with more than 750 patients demonstrated an NAFLD prevalence of 25.8%, with NAFLD rates being higher among males (33.4%).[51] In Germany, a recent cross-sectional, population-based study among almost 15,000 participants reported a prevalence of 37.5%, but it needs to be noted that rather than ultrasound data, the authors defined NAFLD by fatty liver index.[52] The Dionysos nutrition study, albeit about two decades old, demonstrated an NAFLD prevalence of 25% in Northern Italy.[53] In this context, a multicentric study of the Italian Atherosclerotic Society reported that among patients with metabolic syndrome, NAFLD rates were as high as 78%.[54]

Similar rates were reported from the United Kingdom, France, Hungary, and Romania.[28,55]

The prevalence of NAFLD and NASH in Eastern European countries is difficult to estimate not only due to a few epidemiologic studies, but also because of in these countries there exists a unique combination of epidemiologic factors that favor the increase in prevalence of advanced liver diseases and its complications and liver-related mortality. Indeed, it is difficult to evaluate the real prevalence of NAFLD/NASH by screening the population with high consumption of alcohol, high prevalence of viral hepatitis and obesity.

The largest epidemiologic studies among Eastern European countries were performed in Russia, in which the prevalence of NAFLD/NASH was assessed in primary care physicians' patients who visited them for any reason. Abdominal ultrasound, blood tests, and physical examination were performed. Among 30,787 patients who were enrolled into the DIREG1 study in 2007, 24% of patients were found to have liver steatosis, in 3.3% with elevated ALT, and in 0.8% of the studied population liver cirrhosis was found.[56] Six years later, the study was repeated and among 50,145 patients enrolled 28.1% of patients demonstrated liver steatosis at abdominal ultrasonography (US), in 9.1% of patients with elevated alanine aminotransferase (ALT) and in 0.84% with cirrhosis.[57] However, there were serious drawbacks in both studies including the unclear method for assessment of alcohol consumption (as the widely accepted CAGE or Alcohol Use Disorders Identification Test (AUDIT) questionnaires were not used); poor standardization of US protocol (different equipment and operators); and age disproportion between two studies (33% younger than 40 in DIREG1 compared with only 10% in DIREG2). The prevalence of viral hepatitis markers was surprisingly low for the Russian population in the first study (1.8% for HBV and 1.4% for hepatitis B virus [HCV]), and it was not mentioned at all in the second one.

Recently, two population-based studies have been performed (Ural Eye and Medical Study and Ural Very Old Study), in which the prevalence and associated factors of NAFLD were evaluated in rural and urban regions in Bashkortostan, Russia, and included 5852 participants aged 40 + years and 1130 participants of 85 + years, respectively. Defining NAFLD by the absence of consuming alcohol on a regular basis and by abnormally high ALT and aspartate aminotransferase (AST) levels or by an AST/ALT ratio of greater than 1.0, they found that 789/1130 (69.8%; 95%CI 67.1, 72.3) individuals of 85+ years had NAFLD. In multivariable analysis, a higher NAFLD prevalence was associated with female sex (OR 2.24; 95%CI 1.66, 3.01; $P < .001$), higher serum concentrations of low-density lipoproteins (OR 1.34; 95%CI 1.17, 1.55; $P < .001$), lower prothrombin index (OR 0.98; 95%CI 0.96, 0.99; $P = .002$), and lower ankle-brachial index (OR 0.03; 95%CI 0.02, 0.29; $P = .003$).[58] However, in Ural Eye and Medical Study, the prevalence of NAFLD was 2341/5852 or 40.0% (95%CI 38.8, 41.3). In univariable analysis, a higher NAFLD prevalence was associated ($P \leq .10$) with older age, female sex, and non-Russian ethnicity.[58] The major drawback of both studies was the use of only ALT or ALT/AST ratio as the criteria for NAFLD, without exclusion of viral hepatitis, and other numerous reasons for ALT elevation. The absence of regular alcohol abuse was confirmed by questions about alcohol consumption (since when or when stopped, alcohol consumption-related wrongdoing); however, there is no information how it was validated or compared with widely accepted questionnaires or scales used for the evaluation of alcohol consumption.

Conclusions of all four studies should be accepted with caution, as the high alcohol consumption (7–10 L per capita/year) and HCV-infection (4.5–5 million of HCV-positive) are still the major causes of liver steatosis and hepatitis in the population.

However, in all mentioned studies, both factors may be underestimated due to methodological weakness of the study protocols.

Large multicenter observational study (PRELID 2) was performed in 100 medical centers to evaluate the prevalence of NAFLD among patients seeking general practitioners' and gastroenterologists' help in Ukraine. Concomitant pathology, metabolic syndrome, and its individual criteria in patients with confirmed and unconfirmed diagnosis of NAFLD were also evaluated. Among 5000 patients enrolled nonalcoholic steatosis was diagnosed in 3153 (62.72%), NASH—in 1517 (30.30%), and liver cirrhosis—in 44 (0.88%) patients.[59] However, only in 3571 (71.42%) cases, the diagnosis was confirmed, because doctors included in the study the patients with suspected NAFLD. In the presence of metabolic syndrome, the diagnosis of NAFLD was confirmed in 76.07% of cases, with a low level of high-density lipoproteins—in 71.25%, with hypertriglyceridemia—in 77.15%. The results of this study are difficult to extrapolate to the general population as it was performed in tertiary centers (gastroenterology departments), and it is not clear how alcohol consumption and other causes of liver steatosis were excluded in the studied population.

In other Eastern European countries, the prevalence of NAFLD or NASH has not been evaluated in large population-based studies; however, several single-center studies should be mentioned. In Belarus, 548 office workers were enrolled into the study for the assessment of NAFLD risk factors, and in 26% of them, liver steatosis was revealed by US, but in 5.2% presumed NASH was diagnosed by chronic ALT elevation and exclusion of other common reasons of liver inflammation including hepatotropic viruses, drugs, and alcohol consumption.[60] The combination of abdominal obesity, hypertension, and dyslipidemia was found in 90% of patients with liver steatosis and in half of patients with NASH, all other patients with NASH except one were diabetic. Abdominal obesity itself was associated only with 8% of patients with liver steatosis, and it was only a risk factor in one patient with NASH.

In Moldova, there were no specific studies evaluating the prevalence of NAFLD/NASH in the general population, but World health organization (WHO) regularly performed studies evaluating the risk factors for noncommunicable diseases in the frame of STEP survey,[61,62] the results of which can be interesting for defining probable level of prevalence of liver steatosis and NASH in the population. The combined results of reports published in 2013 and in 2020 demonstrate that the prevalence of overweight individuals in the population was 56% and it was increasing with age up to 79.8% in women of 45 to 59 years old, but obesity was found in 26.1% of men and in 45.7% of women of the same age group. More than 58% of middle-aged men and women have raised blood pressure, 19.7%—elevated blood glucose and 42.3%—raised blood cholesterol. Taking it all into account, it can be said that high prevalence of NAFLD/NASH in Moldova looks quite probable. However, the same reports showed that around 70% of men of all ages and 57% of women consume alcohol and at least 30% of men and 10% of women reported heavy episodes of drinking.[62] Viral hepatitis is still prevalent in Moldova,[63] and as a consequence, there is a substantial number of liver cirrhosis and more than 80% of all cases of HCC are related to hepatotropic viruses.[64]

FUTURE PROJECTIONS

Considering that about one third of the world's general population is affected by NAFLD and the epidemiologic trends in obesity, diabetes, and metabolic syndrome have been worsening, the burden of NAFLD and NASH is expected to worsen over the years, not only in developed countries but also in the developing countries. In this context,

research has shifted toward predicting the future impact of these conditions; thus, different Markov models were developed to reliably anticipate the clinical, economic, and total health care burden of NAFLD and NASH in the coming decades. A study by Estes and colleagues used a dynamic model for assessing the future burden of NAFLD for the United States for the year 2030. It was reported that compared with 2015, by 2030, NAFLD population was projected to increase by 21%, NAFLD prevalence to increase by 10% and reach 33.5%, NASH population to increase by 63%, advanced fibrosis (F3/F4) to increase by 160%, compensated cirrhosis to increase by 163%, the number of decompensated cirrhosis to increase by 180%, hepatocellular carcinoma cases to increase by 146%, and liver transplant cases to increase by 59%.[65] However, future projections are not very different for European countries, as models demonstrate that the burden of NAFLD and NASH will continue to worsen. It is estimated that by 2030, the number of NAFLD cases will increase by 13.5% in Germany, and up to 20.2% in the United Kingdom, and NAFLD prevalence will reach 23.6% in France and to 29.5% in Italy.[65] These data as well as data from population-based databases suggest that the prevalence and burden of NAFLD are expected to worsen in the next decades. These alarming statistics require an effective and urgent public health strategy to deal with the pandemic of obesity and related NAFLD.

NONALCOHOLIC FATTY LIVER DISEASE AWARENESS

Despite the rising prevalence and burden of NAFLD/NASH, knowledge and awareness about the disease are still highly suboptimal and unsatisfactory. In this context, raising awareness among patients and health care providers, especially among those in the primary care setting, must become a priority. This increase in awareness must be coupled with programs and algorithms to identify NAFLD patients at highest risk of progression to adverse outcomes (see chapter 14). Unfortunately, the lack of awareness and delays in diagnosis is a major challenge with the majority of cirrhotic patients with NASH present in decompensated state and advanced hepatocellular carcinoma.[66,67] In the context of awareness, both patient and provider and patients and providers' perspectives must be considered.

Patient Knowledge and Awareness

From the patient's perspective, NAFLD can go undiagnosed for years, as symptoms are mild and unrecognized until more advanced stages of liver disease is reached. In many cases, NAFLD is suspected when abnormalities in liver enzyme levels are detected, or fatty infiltration of hepatic parenchyma is detected in ultrasound incidentally.[68–70] Despite this recognition, further assessment is ignored, and patients have a false sense of security that NAFLD is a "benign" disease. A recent study using NHANES database for 2011 to 2016 period demonstrated that only 5.1% of NAFLD patients were aware of having a liver disease; this rate was only 1.8% for non-Hispanic Blacks, and 8.4% for those with a college or higher degree, emphasizing the role of race and education in disease awareness.[68] Another multicenter, prospective cohort study in the United States reported similar findings. Almost 2800 patients with risk factors for coronary artery disease participated in the 25th year of the cohort study, filled out a survey and underwent non-contrast computed tomography of the abdomen.[69] The prevalence of computed tomography (CT)-diagnosed NAFLD was 23.9% in this study, and only 2.4% of the participants were aware of their liver condition. This study did not demonstrate any difference in education levels between NAFLD aware and unaware groups.[69] A recent study compared disease awareness between NAFLD and viral hepatitis and included more than 37,000 subjects.[71] This study demonstrated that even though the prevalence of

NAFLD was considerably higher than viral hepatitis, there were striking differences in disease awareness, as only 4.4% of patients with NAFLD were aware of their liver condition, as opposed to 42.4% of patients with HCV and 17.2% with hepatitis B virus (HBV).[71]

It is certain that NAFLD awareness should be increased in the population level and a study from Brazil may provide some insights in terms of possible ways to achieve this. Almost 2000 individuals participated in a recent population-based survey sponsored by the Brazilian Liver Institute and per the results, NAFLD ranked second as the mostly recognized cause of liver cancer, following alcohol.[72] It can be suggested that social media could play an important role in improving disease awareness.

Clinician Knowledge and Awareness

Besides patients', health care providers also have significant challenges related to NAFLD/NASH knowledge and awareness. Even though NAFLD has been growing at an unprecedented rate, it is estimated that 20% and possibly fewer cases of NAFLD have been diagnosed.[73] Even though routine screening for NAFLD is not recommended by the American Association for the Study of Liver Diseases, it is the primary care level that "at risk" population should be identified and linked to specialty care. In this context, the optimal knowledge and awareness efforts must target the primary care providers and endocrinologists who see the largest number of patients at risk with T2DM and obesity.[74–76]

To illustrate these challenges, a recent global survey of 2202 providers across 40 countries (primary care, endocrinologists, gastroenterologists, and hepatologists) suggested a significant knowledge gap, especially among the primary care physician (PCPs).[77] In terms of knowledge, expectedly, the proportion of correct answers was highest for hepatologists, followed by gastroenterologists, endocrinologists, and primary care providers. Even though 80% of endocrinologists and 66% of primary care doctors reported that they would screen patients for NAFLD if they had diabetes or dyslipidemia, 9.2% of primary care providers reported not screening for NAFLD at all. Interestingly, more than 50% of primary care providers were not familiar with NAFLD fibrosis score and were not aware that cardiovascular disease was the leading cause of mortality among NAFLD cohort.[77] Similar to other reports from different parts of the world, this finding emphasizes the importance of provider training.

Another study from Australia among 108 PCPs provides daunting results.[74] In fact, half of the participants thought NAFLD prevalence was less than 10% in the general population, a quarter of the participants thought liver enzyme levels were sensitive for detecting NAFLD, and 71% stated they were unlikely to refer a patient to hepatology unless liver enzymes were abnormal.[74]Finally, a study from France evaluated the awareness of diabetologists and general practitioners about chronic liver disease.[78] Among a total of 678 providers (500 general practitioners and 178 diabetologists), NAFLD was identified as the main cause of chronic liver disease (CLD) in 36% and as the second most common cause of CLD in another 36%. About 82% of general practitioners and 96% of diabetologists were correct in NAFLD prevalence trends. Interestingly, even though 74% of general practitioners reported being familiar with noninvasive tests, FIB4 was cited by only 15% of them.[78] Similarly, two-thirds of primary care clinicians in Australia were unsure whether FIB4 or enhanced liver fibrosis score could help identifying advanced fibrosis.[74]

These data raise a few questions at different provider settings. "What needs to happen for a simple noninvasive test to be performed at primary care level?" Considering the primary source of knowledge for NAFLD among primary care providers is the

Internet, the answer to this question should be providing online computer-based modules and regular webinars for updates.

Besides the patients' and providers' awareness of NAFLD, it is also worth mentioning the countries' preparedness for the growing global burden of NAFLD. Recent studies clearly demonstrate that no country has a national strategy for NAFLD and only 32 countries have national NAFLD guidelines.[79,80] It is certain that to control the worsening NAFLD burden, there is an urgent need for policy improvements across the globe.

SUMMARY

NAFLD prevalence is increasing all over the world due to rising rates of obesity and T2DM. Future projections estimate that the proportion of NASH and NAFLD will continue to increase, resulting in more patients with advanced stages of liver disease, a rise in hepatocellular cancer cases, and the demand for liver transplantation. In order to combat this daunting clinical and economic burden of NAFLD/NASH, effective programs to raise awareness and identify patients at risk must be undertaken. These efforts must be implemented as national and regional guidelines and policies and should be coupled with the development of new therapeutic regimens for progressive NASH.

CLINICS CARE POINTS

- Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease that affects around 30% of the global population.
- NAFLD is a disease spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), which can progress to cirrhosis, HCC.
- NAFLD and NASH are responsible for the rapidly growing clinical, patient reported outcomes (PROs) and economic burden around the world.
- NAFLD patients with type 2 diabetes (T2D) and other components of metabolic syndrome are especially at high risk for adverse outcomes and should be the main targets of risk stratification and management.
- Awareness of NAFLD is low across all countries There is an urgent need to take public health action to increase awareness of NAFLD.

POTENTIAL COMPETING INTERESTS

Dr Z.M. Younossi is a consultant to BMS, Gilead, AbbVie, Abbott, Novo Nordisk, Merk, Siemens, and Intercept. All other authors have no conflict of interest to disclose.

FUNDING

None.

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