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A Global Survey of Physicians Knowledge About Q2 Q1 Non-alcoholic Fatty Liver Disease

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BACKGROUND & AIMS: Despite rapidly increasing nonalcoholic fatty liver disease (NAFLD) prevalence, providers' knowledge may be limited. We assessed NAFLD knowledge and associated factors among physicians of different specialties globally.

METHODS: NAFLD knowledge surveys containing 54 and 59 questions covering 3 domains (epidemiology/pathogenesis, diagnostics, and treatment) were completed electronically by hepatologists, gastroenterologists (GEs), endocrinologists (ENDOs), and primary care physicians (PCPs) from 40 countries comprising 5 Global Burden of Disease super-regions. Over 24 months, 2202 surveys were completed (488 hepatologists, 758 GEs, 148 ENDOs, and 808 PCPs; 50% high income Global Burden of Disease super-region, 27% from North Africa and Middle East, 12% Southeast Asia, and 5% South Asian and Latin America).

RESULTS: Hepatologists saw the greatest number of NAFLD patients annually: median 150 (interquartile range, 60–300) vs 100 (interquartile range, 35–200) for GEs, 100 (interquartile range, 30–200) for ENDOs, and 10 (interquartile range, 4–50) for PCPs (all $P < .0001$). The primary sources of NAFLD knowledge acquisition for hepatologists were international conferences (33% vs 8%–26%) and practice guidelines for others (39%–44%). The Internet was the second most common source of NAFLD knowledge for PCPs (28%). NAFLD knowledge scores were higher for hepatologists than GEs: epidemiology, 62% vs 53%; diagnostics, 80% vs 73%; and treatment, 61% vs 58% ($P < .0001$), and ENDOs scores were higher than PCPs: epidemiology, 70% vs 60%; diagnostics, 71% vs 64%; and treatment, 79% vs 68% ($P < .0001$). Being a hepatologist or ENDO was associated with higher knowledge scores than a GE or PCP, respectively ($P < .05$). Higher NAFLD knowledge scores were associated independently with a greater number of NAFLD patients seen ($P < .05$).

CONCLUSIONS: Despite the growing burden of NAFLD, a significant knowledge gap remains for the identification, diagnosis, and management of NAFLD.

Keywords: Primary Care; Endocrinologists; Internet; Guidelines; Cardiovascular Disease.

Nonalcoholic fatty liver disease (NAFLD) is a common liver disease.^{1,2} Although the majority of patients with NAFLD do not progress, a proportion of patients with underlying nonalcoholic steatohepatitis (NASH) can progress to advanced liver disease. Globally, NAFLD affects 1 in 5 adults, with higher rates reported from the Middle East and South America.³ The increased global burden of NAFLD is driven primarily by the obesity epidemic.^{4,5} Because of its high prevalence, NAFLD has become a major cause of liver-related mortality and morbidity, and is on track to become the most common indication for liver transplantation in the United States. ^{7,8} Despite its growing burden, it is estimated that less than 20% of patients with NAFLD have been diagnosed.⁹ In addition, health care providers' knowledge about NAFLD is quite limited and varies widely across specialties.^{10–16} In this context, patients with advanced NAFLD or NASH-related cirrhosis are seen primarily in hepatology and gastroenterology practices.^{13,16} On the other hand, most patients who are at increased risk for NAFLD, in particular those with type 2 diabetes and/or visceral obesity, are seen in primary care and endocrinology practices without being recognized as such or being referred for further evaluation.^{11,12} Furthermore, several small or regional studies have found a need for improved understanding of NAFLD and its associated burden.^{13–15} This lack of awareness and

gaps in knowledge about NAFLD may lead to suboptimal identification and management of these patients, which may be responsible for an increasing number of patients presenting with advanced disease. It would be beneficial to identify these patients early to not only optimize their liver health but also their cardiometabolic risks because the majority of patients with NAFLD would die from cardiovascular disease.⁴ Furthermore, as new drugs for the treatment of NASH become available, identification of patients early can lead to potential improvement in patient outcomes. Therefore, our aim was to conduct a large-scale global survey study using a validated tool to assess knowledge about NAFLD among physicians from different medical specialties.

Methods

Two separate NAFLD knowledge and awareness surveys were developed through input and review by participating NAFLD experts from different countries. Those included a 59-item survey for gastroenterology and hepatology specialists and a 54-item survey for endocrinology and internal medicine/primary care physicians. The surveys covered all aspects of NAFLD knowledge and had differences according to relevance to the specialties; 21 questions were overlapped between the 2 surveys. Each question and its answer options were reviewed by participating experts for face and content validity and accuracy. The gastroenterology and hepatology (specialist) version of the survey was completed by hepatologists and gastroenterologists while the other (nonspecialist) version was offered to endocrinologists and internal medicine/primary care providers (PCPs). Members of the Global NASH Council were responsible for distributing a link to the survey web page among physicians in their country. All surveys were completed electronically in English or other national languages (Spanish, Japanese, Turkish, and so forth) via the Survey Monkey website. In addition to questions about NAFLD, survey completers were asked about their demographics (country, age, sex), practice setting (hospital-based, clinic-based, group practice, solo private practice, or other), number of years in practice, the number of patients with NAFLD they typically see in a period of time, and their primary source of knowledge about NAFLD. Countries were grouped based on Global Burden of Disease (GBD) superregions.¹⁷ In addition to a number of questions about physicians' practice and their awareness of NAFLD, 32 questions in the

gastrohepatology version and 24 questions in the nonspecialist version of the survey were multiple-choice questions with only 1 correct answer. Those questions were used to assess physicians' knowledge about NAFLD. Using these questions, NAFLD knowledge scores were calculated as proportions of correct answers (range, 0–100) for 3 knowledge domains: (1) epidemiology and pathogenesis, (2) diagnostics, and (3) treatment, for the specialist and nonspecialist versions of the survey separately. Finally, the total NAFLD knowledge score was calculated as an average of the 3 domain scores.

Statistical Analysis

The answers to the survey were summarized as N (%) or median (interquartile range). The chi-square test and the Kruskal–Wallis test were used to compare categorical and continuous parameters, respectively, between medical specialties. NAFLD knowledge scores were summarized as means (SD) and were compared between specialties using the Mann–Whitney test for the specialist and nonspecialist versions of the survey separately. Independent predictors of the total NAFLD knowledge scores were assessed using generalized linear regression models. In these models, potential predictors of the scores included physician specialty, their practice setting, the number of years in practice, self-reported number of NAFLD patients seen over a period of time, their primary source of knowledge about NAFLD, and their country's GBD super-region. Predictors with a P value less than .05 were considered statistically significant. All analyses were run using SAS 9.4 (SAS Institute, Cary, NC). The study was granted an exemption from consent by the institutional review board because of the nature of the survey content and anonymous reporting.

Results

Demographic Characteristics of the Respondents

During 24 months, 2202 physicians completed the survey. This included 488 hepatologists, 758 gastroenterologists (GEs), 148 endocrinologists (ENDOs), and 808 internal medicine/PCPs. Of the participating physicians, 50% were from the high-income GBD superregion, followed by 27% from North Africa and the Middle East, 12% from Southeast Asia, and 5% from South Asia and Latin America

(Supplementary Table 1). Hepatologists were more commonly from the highincome super-region (58%) while GEs were overrepresented in Southeast Asia (21%) and ENDOs in South Asia (14%). In contrast, PCPs were distributed evenly across the regions. Hepatologists had the longest practice duration and were also the oldest (35.3% were >50 years vs 32.3% of GEs, 25.6% of ENDOs, and 27.6% of PCP) (Table 1). There were no sex differences across the specialties. Hepatologists reported seeing the greatest number of NAFLD patients per year ($P < .0001$). The majority of all providers were affiliated with a hospital (Table 1). The most common primary source of NAFLD knowledge acquisition was international or national conferences for hepatologists (33.4% vs 8% to 25.5% for other providers), while practice guidelines were the primary source for nonhepatology specialties (39.4% to 43.9% vs 26.4% for hepatologists). Notably, the Internet was the second most common source of knowledge for PCPs (28%) (Table 1).

Diagnosis of Nonalcoholic Fatty Liver Disease

Hepatologists and GEs reported significantly higher rates of access to diagnostic modalities for NAFLD (ultrasound or computed tomography, and also liver biopsy) in comparison with nonspecialists (all $P < .0001$). Of these modalities, ultrasound was available to 89.1% of physicians across all specialties while liver biopsy was available to 79.5% of hepatologists and only 27.1% of PCPs (Table 2). Both magnetic resonance imaging–proton density fat fraction and controlled attenuation parameter (CAP) were the least accessible modalities to all medical specialties (Table 2). The most common diagnostic option of choice among hepatologists was hepatic ultrasound and CAP, while hepatic ultrasound alone was the most common choice for all other specialties (Table 2). Interestingly, serum biochemical markers were favored by 15% to 24% of all physicians; the highest rate was observed among ENDOs and the lowest rate was observed among hepatologists (Table 2). Very few (< 7%) used computed tomography scanning or magnetic resonance imaging–proton density fat fraction as the primary method to diagnose NAFLD.

Awareness and Knowledge About Nonalcoholic Fatty Liver Disease

Of all hepatologists, 73.6% believed that very few NAFLD patients (symptomatic (Table 2). Despite a generally low perceived prevalence of symptomatic NAFLD, the vast majority of physicians of all specialties (76%–88%) reported that they believe that NAFLD patients do have an impaired quality of life (Table 2). The

proportion of correct answers was consistently highest among hepatologists followed by GEs, and lowest among PCPs (Table 3). For the GE/hepatology survey version, the mean knowledge scores were higher for hepatologists than GEs: epidemiology/pathogenesis (61.9% vs 53.2%), diagnostics (79.9% vs 73.0%), and treatment (60.8% vs 57.6%) (all $P < .0001$). Similarly, for the nonspecialist version of the survey, ENDOs had higher knowledge scores than PCPs: epidemiology/pathogenesis (70.2% vs 59.7%), diagnostics (70.9% vs 63.8%), and treatment (78.5% vs 67.5%) (all $P < .0001$) (Table 4). In multivariate analysis, adjusted for location and other predictors, being a hepatologist was associated with significantly higher total NAFLD knowledge scores (reference being a gastroenterologist, $b \pm 4.9$ 0.6; $P < .0001$). The other predictors of higher total NAFLD knowledge scores for GE/hepatology were having a practice affiliated with a hospital, seeing a greater number of NAFLD patients per month, and using medical journals or international conferences as the primary source of NAFLD knowledge ($P < .01$) (Table 5). Similarly, being an ENDO (vs PCP) and having a greater number of NAFLD patients in the practice ($P < .01$), but not source of knowledge or the practice setting ($P > .05$), were associated with higher knowledge scores (Table 5). However, for nonspecialists, using the Internet as the primary source of NAFLD knowledge was associated with significantly lower NAFLD knowledge ($b \pm 5.8$ 1.2; $P < .0001$).

Assessment and Management of Nonalcoholic Fatty Liver Disease Among Primary Care and Endocrinology Providers

We asked PCPs and ENDOs about their approach to identification and early stage management of NAFLD patients. As such, 79.7% of ENDOs and 66.2% of PCPs reported they would screen patients with diabetes for NAFLD followed by screening patients with dyslipidemia and unexplained increased alanine aminotransferase levels (Table 6). Only 27.0% of ENDOs and 20.2% of PCPs reported they would screen everyone for NAFLD while 9.2% of PCPs reported not screening for NAFLD at all (vs <1% ENDOs) (Table 6). Approximately 5% of all physicians (3% ENDOs) reported that they would do nothing if they incidentally found fatty liver on imaging (Table 6).

On the initial assessment of patients with suspected NAFLD, 64.9% of ENDOs and 55.0% of PCPs would try to exclude other liver diseases. Furthermore, more than half of ENDOs would send NAFLD

patients for a biopsy only if they were believed to be at risk for steatohepatitis and cirrhosis (56.8%) or if other causes of liver disease could not be excluded (58.8%). Those numbers for PCPs were 51.9% and 47.5%. Nearly half of the survey completers would order a liver biopsy for a patient with a high NAFLD Fibrosis Score (Table 6). There were more ENDOs compared with PCPs (37.4% vs 28.0%) giving pharmacotherapy to patients with NAFLD. Furthermore, between 77% and 80% reported that they would refer their NAFLD patients to a specialist (GE/hepatologist), especially if they identified them to be at risk for steatohepatitis or cirrhosis (72%) or as having a high NAFLD Fibrosis Score (50%) (Table 6). The most common reported barrier to NAFLD management among nonspecialists was failure of patients to adhere to lifestyle modifications (33.9%). PCPs were more likely to report a lack of confidence in managing NAFLD as a barrier (27.4% vs 14.3%), and both specialty groups reported the lack of effective drugs as another barrier (Table 6).

Assessment and Management of Nonalcoholic Fatty Liver Disease Among Gastroenterologists and Hepatologists

Among GEs and hepatologists, approximately 1 in 3 reported that the majority (>50%) of their NAFLD patients have normal liver enzyme levels. The vast majority of these specialists (GEs, 68.2%; hepatologists, 77.0%) also reported that they send very few (<10%) NAFLD patients for a liver biopsy (Supplementary Table 2). Although more than half of GEs/hepatologists adhered to the guidelines and reported sending their NAFLD patients for a liver biopsy if they had other liver diseases that potentially could co-exist with steatohepatitis, less than half would do so for high non-invasive markers of fibrosis. Even fewer GEs/hepatologists would send their patients for a biopsy for the presence of metabolic syndrome. Finally, both GEs and hepatologists reported that most of their NASH patients (41.3%–48.2%) have stage 2 fibrosis while only 4% of NASH patients had cirrhosis at the time of liver biopsy (Supplementary Table 2).

Discussion

In this study, more than 2200 physicians from across the world completed an extensive survey about their knowledge and awareness of NAFLD as well as approaches to its management. As expected, our

data show that hepatologists see the largest number of NAFLD patients per year while PCPs report seeing the fewest. Although this likely represents referral patterns for patients with NAFLD, it also reflects significant underdiagnosis of NAFLD in the primary care setting, where a large number of patients with risk factors for NAFLD (diabetes, hypertension, visceral obesity) likely are seen.^{3,4} Therefore, these data support targeted education of PCPs to identify patients with NAFLD and to link those at risk for adverse outcomes to specialty care for further evaluation.¹⁸ The most commonly used modality for the diagnosis of NAFLD was hepatic ultrasound alone or in combination with CAP, which conforms with practice guidelines.¹⁸ This likely reflects the wide availability of ultrasound as well as its convenience and cost. CAP was preferred in combination with ultrasound by GEs/hepatologists, who were more likely than PCPs to have these tests available. We also noted that up to 24% used scoring systems based on serum biochemical markers to diagnose NAFLD; however, these scoring systems have been validated only for screening in population studies that lacked imaging data and not in clinical practice.^{19,20} This finding provides another opportunity for health care providers' education. With respect to the presentation of patients with NAFLD, GEs/hepatologists were more likely to say that the majority of NAFLD patients were asymptomatic. This further indicates that PCPs may tend to underdiagnose NAFLD in their patients. Nevertheless, the majority of providers still believe that NAFLD patients have an impaired quality of life, which is consistent with data from clinical trials.^{21–23}

Notably, more than 50% of PCPs were not familiar with the NAFLD Fibrosis Score, were not aware that cardiovascular disease was the leading cause of death in NAFLD patients, and were not familiar with NASH pathologic criteria. Because PCPs play an important role in the management of NAFLD metabolic risks, education to aggressively manage these comorbidities as well as to refer patients at high risk for NASH to specialty care likely will be beneficial. In this context, it is important to note that even among specialists some aspects of NAFLD knowledge were quite far from perfect; for example, roughly 1 in 3 hepatologists could not correctly identify NAFLD Fibrosis Score as a noninvasive test that is based on routine clinical and laboratory parameters even though the only alternative answer options were that it was a histologic score or a liver stiffness measurement. Notably, the primary source of knowledge about

NAFLD was an independent predictor of knowledge scores among both specialists and nonspecialists. In this context, it is important to note that PCPs commonly relied on the Internet as their primary knowledge source, and this reliance had an inverse association with their total NAFLD knowledge score. This highlights the need to deliver accurate information about NAFLD to PCPs through online computer-based teaching modules and regular webinars on new updates. Finally, there were regional differences in knowledge among nonspecialists (those practicing in the Middle East/North Africa region), which can be used to provide more targeted educational programs for those doctors. The wide variance in physicians' responses regarding NAFLD screening methods reflects considerable heterogeneity of current practice guidelines. Indeed, AASLD does not recommend any screening at this time.¹⁸ In contrast, the EASL, EASD, and EASO joint guideline recommends that screening should be a part of routine work-up in patients with diabetes and metabolic syndrome.²⁴ The Asia-Pacific Working Party on NAFLD states that screening should be considered in at-risk populations such as patients with overweight/obesity, type 2 diabetes mellitus, and metabolic syndrome.²⁵ The 2019 American Diabetes Association Standard of Care Guidelines recommend that patients with type 2 diabetes mellitus and increased alanine aminotransferase levels or fatty liver on ultrasound should be evaluated for the presence of NASH and liver fibrosis.²⁶ These differences in screening recommendations could be owing partly to the lack of data about the impact of screening for NAFLD to outcomes, the cost utility of screening, and also variability in how each society assesses evidence to make its recommendations. We believe all major societies should come together to harmonize recommendations about screening to inform providers on the front lines who see patients at risk for NAFLD. The role of alcohol consumption in NAFLD/NASH diagnosis is an area that requires clarification. Only slightly more than 50% of physicians would investigate the presence of excessive alcohol consumption among patients who incidentally were found to have fatty liver on imaging despite the requirement to exclude excessive alcohol use before diagnosing NAFLD.^{27,28} This finding is consistent with a French study in which up to 21% of practicing gastroenterologists would diagnose NASH even in patients consuming more than 40 g/d among men and more than 30 g/d among women.¹³ Another area needing further clarification is the role and use of liver biopsy among patients with NAFLD. Our data showed that the vast majority of providers rarely send their NAFLD patients for a liver biopsy, although approximately 10% of

PCPs and endocrinologists would use liver biopsy as the initial assessment of patients with suspected NAFLD while less than 5% of GEs/hepatologists may not send their NAFLD patients for a liver biopsy despite the presence of fibrosis risk factors. Unfortunately, we were unable to determine why providers would not send patients for a liver biopsy per guideline recommendations, although the cost and invasiveness and lack of highly effective medications for NASH are likely reasons. On the other hand, the majority of PCPs and endocrinologists (77%–80%) reported that they refer their NAFLD patients to GE/hepatology specialists, rates similar to those reported previously in the United States (52%–79%)^{12,29} and higher than outside the United States (47%–62%).^{13,14} The major study strength was the large international sample of specialists and nonspecialists who completed the survey. This provides a unique opportunity for an indepth exploration of knowledge, awareness, and practices about NAFLD worldwide. The study limitations included a possible bias toward specialists and PCPs interested in and familiar with NAFLD, as well as those who are hospital-based, however, because the number of invitations to the survey that was sent was not centrally recorded, it is hard to determine the magnitude of that bias. However, the major findings on knowledge, awareness, and behavior were not substantially different from other published surveys. In conclusion, we have shown a significant knowledge gap about NAFLD between medical specialties, especially among PCPs and, to a smaller extent, endocrinologists. Because these providers are at the front line of seeing patients with NAFLD, targeted educational programs that would cover those who are most at risk for NAFLD are warranted. Education on alcohol consumption and liver biopsy and their role in NAFLD diagnosis likely would be beneficial among all providers.

Tables

Table 1. Demographics of Participating Physicians

IQR, interquartile range; NAFLD, nonalcoholic fatty liver disease.

Table 2. Availability of NAFLD Diagnostic Methods and NAFLD Awareness Among Physicians of Different Specialties

AASLD, ____; APASL, ____; EASL, ____; ENDO, endocrinologist; GE, gastroenterologist; MRE, ____; MRI-PDFF, magnetic resonance imaging–proton Q18 density fat fraction; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; PCP, primary care provider.

Table 3. Knowledge About NAFLD Across Medical Specialties

NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

Table 4. NAFLD Knowledge Scores Across Medical Specialties

NOTE. The scores were calculated separately for the specialist and nonspecialist versions of the survey using different subsets of questions and are not directly comparable between the 2 versions besides questions included in Table 3. NAFLD, nonalcoholic fatty liver disease; PCP, primary care provider.

Table 5. Independent Predictors of NAFLD Knowledge Scores From Generalized Linear Regression Models

NAFLD, nonalcoholic fatty liver disease a The specialty predictor is coded as follows: hepatologist (reference: gastroenterologist) for the specialist version of the survey, endocrinologist (reference: primary care provider and other) for the nonspecialist version.

Table 6. Survey of NAFLD Practice Among Completers of the Nonspecialist Version of the Survey

ALT, alanine aminotransferase; CT, computed tomography; MRI, magnetic resonance imaging; NAFLD, nonalcoholic fatty liver disease; PCP, primary care provider.

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