Review

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From NAFLD in clinical practice to answers from guidelines

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Summary

This review of the literature consists of three sections.

First, papers concerning non-alcoholic fatty liver disease (NAFLD) awareness among the general population, general practitioners, and liver and non-liver specialists were retrieved and analyzed to highlight the perception of disease, verify knowledge of current recommendations, and identify the main difficulties experienced in clinical practice.

Next, position papers and clinical practice guidelines issued by International and National Hepatological Scientific Societies were identified and critically assessed in order to pinpoint the areas of convergence/difference.

Finally, practical suggestions on NAFLD diagnosis and management in daily practice are provided and the open questions highlighted.

Introduction

Non-alcoholic fatty liver disease (NAFLD), the hepatic counterpart of the metabolic syndrome (MS) [1,2], encompasses a disease spectrum spanning steatosis through non-alcoholic steatohepatitis (NASH) with/without cirrhosis, and hepatocellular carcinoma (HCC) [3]. The obesity and type 2 diabetes (T2D) pandemic and the improved management of chronic viral hepatitis have resulted in NAFLD becoming a leading cause of chronic liver disease (CLD) [4] and a major health concern owing to hepatic and extrahepatic morbidity/mortality [5–7].

Such a shift in the epidemiology of CLD has left practicing clinicians somewhat puzzled in identifying and treating this NAFLD "epidemic" [8–12]. Moreover, an ever increasing number of practice guidelines on NAFLD diagnosis and management issued by eminent Scientific Societies may probably add to the uncertainties concerning the best conduct to follow in clinical practice.

Our paper aims at (1) highlighting the perception of NAFLD among practicing physicians, (2) providing a critical, comparative analysis of the statements on NAFLD diagnosis and management, issued by clinical practice guidelines and technical reviews of Scientific Societies, (3) offering practical suggestions on the controversial topics and defining the unsettled questions.

Methods

We conducted a PubMed database search (keywords: general practice and/or primary care and/or specialists and/or physicians and/or awareness and/or perception and/or liver steatosis and/or fatty liver and/or NAFLD and/or NASH and/or guidelines and/or recommendations. Limits: December 2012 and English language) aimed at ascertaining: (a) the awareness/perception of the importance of NAFLD-NASH among potential patients and practicing physicians [both general practitioners (GPs) and specialists] and (b) guidelines/consensus/recommendations for NAFLD diagnosis and management issued by Medical Societies.

Six studies meeting the inclusion and exclusion criteria investigated current beliefs and practices of NAFLD among the general population, GPs and liver and non-liver specialists [8–13]. Moreover, three further studies [14–16] addressing the clinical approach of practicing physicians towards pediatric NAFLD were identified (Table 1).

Five position papers and clinical practice guidelines, issued by the European Association for the Study of the Liver (EASL) [17], Asian-Pacific Working Party for NAFLD (APWP-NAFLD) [18], Chinese Liver Disease Association (CLDA) [19], Italian Association for the Study of the Liver (IASL) [20] and American Gastroenterological Association (AGA)-American Association for the Study of Liver Disease (AASLD)-American College of Gastroenterology (ACG) [21], were identified. Three out of five such reports are evidence-based [19–21]. A single position paper on diagnosis of

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Abbreviations: NAFLD, non-alcoholic fatty liver disease; MS, metabolic syndrome; NASH, non-alcoholic steatohepatitis; HCC, hepatocellular carcinoma; T2D, type 2 diabetes; CLD, chronic liver disease; GPs, general practitioners; EASL, European Association for the Study of the Liver; APWP, Asian-Pacific Working Party; CLDA, Chinese Liver Disease Association; IASL, Italian Association for the Study of the Liver; AGA, American Gastroenterological Association; AASLD, American Association for the Study of Liver Disease; ACG, American College of Gastroenterology; ESPGHAN, European Society for Pediatric Gastroenterology, Hepatology and Nutrition; LB, liver biopsy; US, ultrasonography; IR, insulin resistance; MRFs, metabolic risk factors; AFLD, alcoholic fatty liver disease; LTs, liver tests; CVD, cardiovascular disease.

Table 1. Analysis of reports from real-life clinical practice.

Author, yr [Ref.]	Methods	Main findings
Leung CM, *et al.*, 2009 [13]	Telephone survey on NAFLD knowledge among 521 subjects randomly selected from the general population in Hong Kong.	Among those interviewed, 83% had never come across the term "NAFLD." Among those who had heard of NAFLD, 42% had no idea about prevalence, 47% knew nothing about clinical presentation, 78% thought that blood tests could provide definite diagnosis, about 50% mistook associated risk factors and 81% perceived their knowledge of NAFLD as inadequate.
Grattagliano I, *et al.*, 2008 [8]	Online questionnaire and clinical survey about NAFLD knowledge and management before and after attending a teaching workshop among 56 GPs in Italy.	Before/after teaching workshop - Questionnaire (%): 4.7/42.7 indicated NAFLD as the first cause of undefined persistent hypertransaminasemia, 70/<10 underestimated NAFLD prevalence in general population, 36.6/76.2 would screen diabetic subjects, 39.5/100 should make diagnosis after exclusion of all other causes of liver steatosis, 23.2/61.9 should manage NAFLD patients with diet and a new check after 6 months, 2.3/80.9 should ask for LB in over 50 diabetic patients with persistent hypertransaminaseima, 78/91 indicated diet as the first approach. 34.1% should avoid statins. Practice check: improvement in screening of risk patients, searching for NASH and managing NAFLD.
Loguercio C, *et al.*, 2011 [10]	5-yr retrospective analysis from 104 GPs and 6550 patients with CLD in Italy.	Drinking habits registered in only 20.4% of CLD patients. 81.9% of patients with undefined CLD were overweight/obese. In patients with liver steatosis (NAFLD + AFLD): alcohol consumption recorded in 30.2%, BMI recorded in 59.5%, US performed in 37.9% of patients. No record of additional tests including insulin, HOMA index, ferritin, GGT, lipids and HBV- HCV markers.
Kallman JB, *et al.*, 2009 [9]	Survey questionnaire about screening for HBV, HCV and NAFLD among 103 GPs, 59 gastroenterologists and 52 hepatologists in USA.	Compared to specialists, GPs significantly less likely to be aware of official guidelines, to rate NAFLD as a common cause of liver disease, to screen for NAFLD in asymptomatic patients with diabetes but believed more strongly that available treatments for NAFLD are effective. Hepatologists endorsed appropriate screening scenarios more frequently than gastroenterologists and GPs.
Bergqvist CJ, *et al.*, 2012 [11]	Face-to-face questionnaire assessing beliefs and practices regarding NAFLD among 100 non-liver specialists in Australia.	75% underestimated the prevalence of NAFLD in the general population and 89% in high-risk patients. 57% considered alcohol consumption to be strongly associated with NAFLD. 60% deemed simple steatosis to confer excess liver-related mortality. 66% thought that NASH can be diagnosed with liver imaging. 71% made no referrals to hepatology services for suspected NAFLD.
Ratziu V, *et al.*, 2012 [12]	Survey assessing the clinical burden, perceived severity, and management patterns of NAFLD among 352, board-certified, hepato-gastroenterologists in France.	Most NAFLD patients were referred by GPs and only 20% by specialists. Conversely, 87% of hepatologists referred NAFLD patients for specialistic evaluation of potential co-morbidities. 65% would diagnose NASH irrespective of the concurrent CLD due to other etiology if MRFs were present. No agreement on the threshold of daily alcohol consumption that rules out NASH. Most physicians would overrate the importance of raised transaminases for the diagnosis of NASH. 62% delay LB after diet and lifestyle changes. 90% used non-invasive fibrosis markers. Roughy half did not measure fasting insulin/HOMA, 22% did not measure waist circumference. 73% monitored NAFLD patients themselves; most with yearly US and only 16% with fasting insulin/HOMA. 72% of patients were treated with non-pharmacological measures, often following referral to the endocrinologist/nutritionist. 42% recommended total abstinence from alcohol. Drugs treatment (metformin, UDCA, venesection, glitazones and vitamin E) was prescribed in only 28% of NAFLD patients.
Fishbein M, *et al.*, 2005 [15]	Analysis of physical examination findings and requests for diagnostic testing of 18 physicians involved in pediatric primary care on 11 obese children (4 with NAFLD) in USA.	Hepatomegaly was identified in 0.5% of obese children. Most commonly performed laboratory tests: fasting blood glucose (23%), lipid profile (20%), thyroid function tests (10%), and LTs (8.6%). Most common consultations: dietary (46%) and endocrinology (16%). Exercise program recommended in 4%. Abdominal imaging was requested in none of the encounters. In obese children with NAFLD, clinicians detected hepatomegaly in only 1.4% and requested LTs in 12.5% of encounters.
Sivertsen LM, *et al.*, 2008 [14]	Questionnaire assessing attitudes on diagnosis and management of overweight/obese children and awareness of clinical practice guidelines among 137 GPs in Australia.	The guidelines on the management of childhood obesity in general practice were reported to be used by 30% of respondents. 9% of GPs used BMI charts to correctly diagnose childhood obesity. 30% assessed for fatty liver in overweight/obese children. Over 80% of prescribed interventions were consistent with guidelines.
Riley MR, *et al.*, 2005 [16]	Retrospective chart review of 2256 pediatric outpatient visits at 2 academic hospitals (general pediatricians, pediatric endocrinologists and gastroenterologists) in USA.	Children with BMI 85 to 89%, 90 to 94% and ≥95% were given a diagnosis of overweight during 4, 8 and 48% of visits, respectively. General pediatrics, pediatric endocrinology and gastroenterology visits of overweight children included NAFLD screening in 2, 10 and 23% and metabolic screening in 8, 34 and 3% of cases, respectively.

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