

Improving Nonalcoholic Fatty Liver Disease Management by General Practitioners: a Critical Evaluation and Impact of an Educational Training Program

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Abstract

Background/Aims. The epidemic diffusion of nonalcoholic fatty liver disease (NAFLD) represents an emerging problem in family medicine. General Practitioners (GPs) should pay attention to patients with fatty liver, look at associated conditions, identify causal factors and patients at risk of evolution. This study aimed to assess GPs' knowledge and practice and a training project impact about NAFLD. **Methods.** 56 GPs filled a questionnaire before and after attending a tailored workshop on NAFLD, and performed a clinical survey in patients with persistent hypertransaminasemia including screening and liver biopsy when indicated. Four months after a training workshop, GPs were questioned again about their practice changes with NAFLD. **Results.** At baseline, less than 30% of GPs considered NAFLD as a cause of persistent hypertransaminasemia; over two-thirds thought that NAFLD had a prevalence of 5-10% in the general population;

about 50% considered hypertransaminasemia as the main indication for liver biopsy in NAFLD; their main approach included a low lipid-content diet. Comparison of pre/post workshop questionnaires showed significant improvements, despite knowledge on diet composition and steatogenic drugs remained poor. Among screened patients with hypertransaminasemia, NAFLD had a prevalence of 36% and was associated with the metabolic syndrome in more than 50%. Liver biopsy was obtained in 8% of NAFLD. Chronic viral hepatitis was better diagnosed than NAFLD (biopsy performed in 86% of cases). The training workshop resulted in practice changes concerning screening of risk patients, search for NASH and managing NAFLD in chronic viral hepatitis. **Conclusions.** GPs' knowledge about NAFLD appears barely adequate, thus targeted training is essential to improve their knowledge and practice.

Key words

Audit – educational meeting – liver steatosis – management appropriateness.

Introduction

Liver steatosis is the most frequently diagnosed chronic liver disease [1]. It is often discovered by abdominal ultrasonography performed for persistent elevation of liver enzymes or other unrelated conditions [2, 3]. The form that looks like alcoholic liver disease, but occurring in people who drink little or no alcohol, is called nonalcoholic fatty liver disease (NAFLD) and represents an emerging health problem with an estimated prevalence of 20% to 40% in the general adult population, and with a higher prevalence among obese and diabetic people [4, 5]. Erroneously seen in the past as a benign condition, NAFLD has the potential to progress through the inflammatory phase of nonalcoholic steatohepatitis (NASH) to fibrosis, which accounts for about 5% of NAFLD [6] and may represent a significant proportion of cryptogenic cirrhosis [7]. For every 1,000 patients they see, general practitioners (GPs) are likely to encounter more than 300 cases of NAFLD and 10 to 20 cases of NASH.

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Although NAFLD has no definite biochemical markers or peculiar clinical signs and, at present, there are no diagnostic and therapeutic guidelines, it is important to identify it, to manage risk factors for NASH, and to consider treatment [8, 9]. Having NAFLD worsens the prognosis of other chronic liver diseases and in particular of patients with chronic viral hepatitis, representing a factor of disease progression and treatment resistance [10].

The goal to reduce the number of people living with NAFLD could not be achieved without the contributions of public health, specialty care and especially general practitioners (GPs). In fact, NAFLD patients can usually be managed in family medicine and referral to consultants is indicated to assess the need for liver biopsy or concurrent illnesses. GPs, who constitute more than half of primary health care and outpatient services in Italy, are therefore expected to have basic knowledge of NAFLD. They are supposed to guide their patients appropriately in terms of analysis of their disease and treatment, and be able to identify high-risk groups at an early stage. The GPs' role is also to help patients identify their objectives and goals, to develop management plans and to reach therapeutic targets [8, 11, 12]. Hence, to care for these patients, it is important to ensure that GPs have sufficient knowledge regarding this relatively newly recognized entity. Educational projects in this area would be helpful to consolidate knowledge and to correct inappropriate positions, as previously shown for other chronic liver disease conditions [13, 14].

The objective of this study was the evaluation of the knowledge, the current practices and attitude of GPs regarding NAFLD, and the impact of a training workshop on knowledge and competence.

Methods

In February 2007, a questionnaire (Table I, Addendum) with 14 multiple choice questions concerning epidemiology, clinical impact, diagnosis, evolution, diet and treatment of NAFLD, including also different management options for a typical case was administered online to 56 GPs connected by a network to a GPs' educational portal in Apulia, a region in southeastern Italy. The same questionnaire was completed again in June 2007 after a full day teaching workshop on management of NAFLD patients. Participants were asked not to leave questions unanswered. The questionnaires were not validated. In parallel, a survey on current medical practice was conducted between March and May 2007. GPs were invited to fill anonymous patients' cards containing relevant multiple choice questions on sources of medical information, general clinical information, biochemical data, diagnostic approach and treatment option of patients presented at their office with a persistent hypertransaminasemia. Four months later, GPs were asked about their training initiative induced practice changes by asking to fill online a questionnaire (Table II, Addendum) with five open questions.

Statistical Analysis

Results are expressed as percentage. Categorical variables were compared using a χ^2 test. A *p* value of 0.05 or below

was considered statistically significant. Correct responses were determined by consensus of GPs, hepatologists and internists.

Results

The involved GPs were 16 (28.6%) women and 40 (71.4%) men with a mean age of 51 ± 5 years and having 18 ± 8 years of practice.

Questionnaire

Epidemiology and Screening

With regard to the first cause of an undefined persistent hypertransaminasemia, 48.8% of GPs answered a hepatitis virus and only 4.7% indicated a metabolic cause. After the workshop, 42.7% of GPs indicated a metabolic alteration as the possible cause. Concerning the prevalence of NAFLD in the general adult population, GPs (70%) stated 5-10%; after the workshop 90.5% of them answered 20-40% ($p < 0.05$). About the most frequent condition associated with NAFLD, GPs answered the metabolic syndrome (71% and 76.2% before and after the workshop, respectively). To the question on which subjects they would screen for NAFLD, GPs answered diabetic subjects (36.6% and 76.2% before and after the workshop, respectively) ($p < 0.05$) (Fig. 1).

Definition and Diagnosis

Concerning the definition of NAFLD, 65.1% and 100% GPs decided for fatty degeneration of hepatocytes in patients with an altered glucose or lipid metabolism on pre and post-workshop questionnaire, respectively ($p < 0.05$). To the specific question on how GPs should make diagnosis of NAFLD, 39.5% of them answered after exclusion of all the other causes of liver steatosis, 27.9% by ultrasonographic image of fatty liver in patients with elevation of serum triacylglycerols and/or cholesterol levels, 20.9% by elevation of at least one amino transaminase plus ultrasonography imaging of fatty liver, and 11.6% by liver biopsy and histology. At the second opportunity, 100% GPs answered after exclusion of all other causes of liver steatosis.

Management

Regarding the answers given by GPs on the question: "how do you approach a NAFLD patient?", 41.7% answered diet and a further check after one month, 32.6% searched first for associated conditions, 23.2% diet and a new check-up after 6 months while 2.3% directly referred their patients to the specialist. After the workshop, 61.9% of them chose diet and a new check after 6 months ($p < 0.05$) (Fig. 1). The chosen option for over 90% of the GPs as a reason for a specialist referral was patients with another concomitant liver disease. Among specialists, internists and gastroenterologists were chosen by 95%. GPs indicated high serum transaminase levels (58.2%), over 50 years diabetic patients (2.3%) or none (39.5%) as the best reason to ask for a liver biopsy in a NAFLD subject. After the workshop, 80.9% indicated over 50 diabetic patients with long history of transaminase elevation (Fig. 1).

Treatment and Recommendations

Forty-four (78%) and 51 (91%) of GPs (before and after

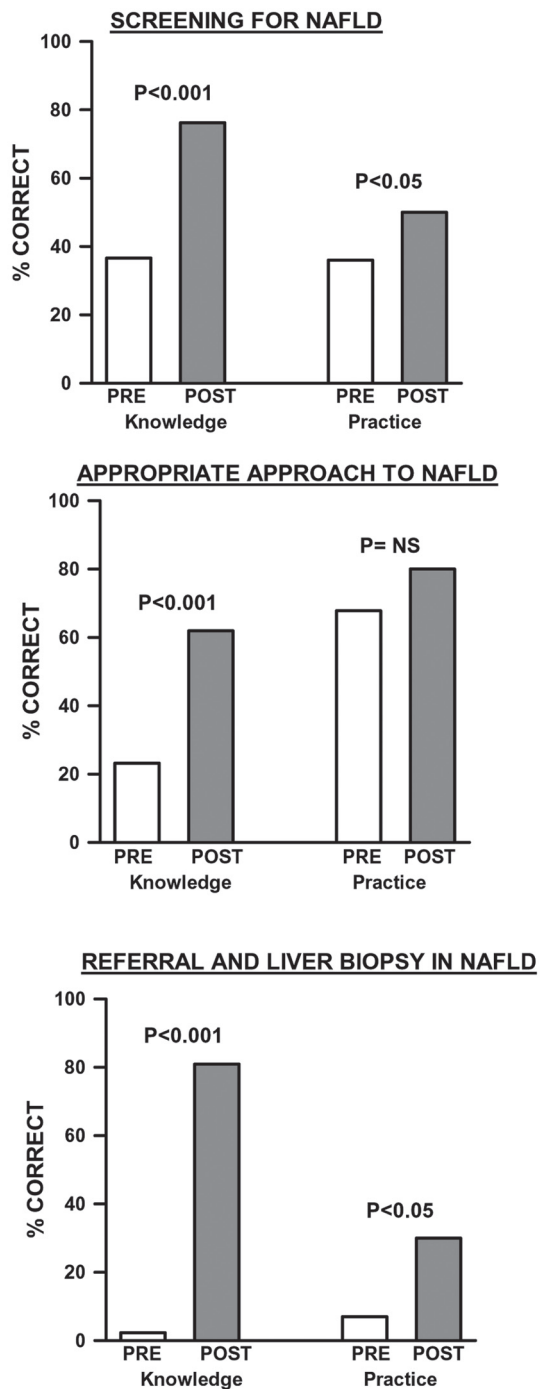


Fig 1. Changes of knowledge and current practice in screening for NAFLD in at risk patients, approach to NAFLD patients, and asking for specialist referral and liver biopsy in patients with a suspected NASH. Values represent the percentage of GPs correctly answering to the specific questionnaire about knowledge (left side) and daily practice (right side). Empty and grey bars report values emerging from pre- and post-training evaluations, respectively.

the workshop, respectively) ($p < 0.05$) indicated diet as the first and best approach to NAFLD. Before the workshop, 52.4% of GPs indicated a low-lipid content diet and 9.5% a low carbohydrate content diet as the best regimen for NAFLD. On the second chance, 47.6% chose the low

carbohydrate diet. From the first questionnaire no clear indications emerged on which medications should be avoided in NAFLD patients. On the second occasion, 61.9% of GPs indicated that hepatotoxic drugs and steatogenic medications should be avoided in NAFLD patients. No clear position emerged for statins which should be anyway avoided for 34.1% of GPs.

Analysis of patients' cards

Between March and May 2007, 212 patients ($n=133$ males) met their GPs and were scheduled. Patients' age was 57 ± 15 years. Serum transaminases elevation was known since 10 years or even more in 113 patients, 5 years in 81 patients and one year in 18. Diagnosis of NAFLD was clearly indicated for 78 patients (36%), however most of them were probable but not confirmed and most GPs agreed that once they had excluded other causes of hypertransaminasemia, suspicion of NAFLD did not necessitate histological confirmation. Alcohol intake was not always correctly investigated and excessive amount could not be excluded in at least $n=7$ cases. Conversely, NAFLD was not considered in at least 37 subjects with high transaminase levels presenting with obesity or diabetes. It also emerged that NAFLD was often accompanied by the metabolic syndrome ($>50\%$) especially when the IDF diagnostic criteria were used (66% vs 57% ATP-III, $p=ns$). Patients with chronic viral hepatitis ($n=77$) were earlier and more appropriately diagnosed than NAFLD: liver biopsy had been performed ($n=42$) with the viral etiology as indication in 86% of the cases. In those patients showing also fatty liver on ultrasonography, NAFLD was rarely considered (8%).

Practice Check

While 20% of GPs indicated that the workshop stimulated a more extensive investigation on hepatic function in their NAFLD patients, 40% declared that they better searched for NASH, and 40% investigated life styles (Fig. 1). 50% of GPs declared to have searched for NAFLD by ultrasonography and serum transaminases in patients presenting with diabetes, obesity or altered lipid levels, while the rest searched for a NAFLD among chronic viral hepatitis patients (Fig. 1). 50% of GPs asked for consultant in 30% of their previously diagnosed NAFLD patients because they now were considered at potential risk of NASH (Fig. 1). Considering treatment, all GPs indicated that the workshop stimulated a profound revision of the cases of chronic viral hepatitis presenting with liver steatosis. More attention to life style modification and diet was proposed to NAFLD patients, reserving medication only as a second step.

Discussion

The current study was designed to evaluate understanding and practices of NAFLD by GPs in an Italian accredited training program and performed with a representative Italian GPs sample which reflected for age and years of practice the average Italian practice. Therefore, our results could be extrapolated to the whole of Italy on the basis of educational levels and working conditions.

General practitioners showed barely adequate basic knowledge and demonstrated sufficient practicing within current recommendations regarding NAFLD, although training necessity emerged from the online audit and the analysis of patients' cards. Following the educational workshop, a significant improvement in the percentage of correct responses exceeding 80% was reported. In particular, the importance given to insulin resistance as a major pathogenic mechanism of NAFLD led most GPs to change the answer on the screening question from obese to diabetic subjects. The knowledge on hepatotoxic drugs was improved but still remained unsatisfactory. The therapeutic role of the diet was well established in the management of these patients; however, over 50% of GPs remained uncertain about its composition, suggesting the need for a more in-depth session.

Indeed, the ideal diet for NAFLD should reduce fat mass and inflammation, restore insulin sensitivity, and provide low amounts of substrates for de-novo lipogenesis, but scientific evidence currently lacks for the recommendation of specific diets. Low-calorie diets with reduction in saturated fatty acids and increase in mono and polyunsaturated fatty acids appeared to be beneficial in some studies. However and in particular, excessive consumption of high glycemic index carbohydrates appears deleterious, as it favours hyperglycemia and hyperinsulinemia and stimulates de-novo lipogenesis (15). In fact, high-glycemic index foods have been related to increased hepatic fat in both rodents and humans. Similarly, simple carbohydrates stimulate hepatic de-novo lipogenesis and decrease lipid oxidation, thus leading to increased fat deposition. Fat intake leads to hepatic fat deposition in animals but few data are available in humans with the role of fat remaining controversial (16). Therefore, although clinical studies showing the benefit of a low carbohydrate diet in NAFLD patients are lacking, our indication was to recommend it if insulin resistance existed.

Our training initiative stimulated GPs toward a more extensive investigation on hepatic function, search for NASH, and promotion of life style changes in their patients. The search for NAFLD was correctly performed by ultrasonography and serum transaminase determination, and extended to all the patients presenting with diabetes, obesity or altered lipid levels. As a consequence, 50% of GPs asked for a consultant in 30% of their previously diagnosed NAFLD patients because they were successively considered as potential NASH. Considering treatment, GPs indicated that the workshop stimulated a profound revision of chronic viral hepatitis presenting with liver steatosis. More attention to life style modification and diet was proposed by them to NAFLD patients, reserving medication only as a second step.

The analysis of the patients' cards suggests several opportunities for improvement. From these data it emerged that NAFLD was often accompanied by the metabolic syndrome especially when the IDF diagnostic criteria were used (3,17). However, most diagnoses of NAFLD

were probable and not confirmed; alcohol excess was not appropriately investigated or not definitely excluded in some cases. By comparing the approach to NAFLD and viral hepatitis patients, some interesting differences emerged. Generally, patients with chronic viral hepatitis underwent an earlier and more accurate diagnosis than NAFLD: liver biopsy had been performed for the presence of hepatitis virus as indication in most cases, and in those patients who also showed fatty liver at ultrasonography, the presence of NAFLD was rarely considered both by GPs and consultants. This approach does not advantage patients, because liver steatosis is a known worsening factor for chronic hepatitis C [18]. This point is of particular interest, since GPs indicated that NAFLD was the best reason to review viral hepatitis patients.

In **conclusion**, GPs showed barely adequate knowledge about NAFLD. Training initiatives about appropriateness of diagnosis and treatment of NASH in particular, should be promoted during post-graduation period with audit initiatives and educational projects [19]. However, at this time, we only assessed knowledge early after completion of the educational session and, clearly, such a testing regime does not address knowledge retention.

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Conflicts of interest

None to declare.

Addendum

Table 1. Pre- and post-workshop questionnaire investigating knowledge about patients with high transaminase levels and/or NAFLD.

1. How do you manage a patient with a persistent undefined hypertransaminasemia?
 - a. Ask for liver ultrasonography
 - b. Check for HBV and HCV infection
 - c. Register data in the patient's card and check it again in one month
 - d. Check for metabolic alterations
 - e. Refer the patient to a specialist
2. What is the prevalence of NAFLD in the general adult population?
 - a. 5%
 - b. 5-10%
 - c. 20-40%
 - d. 50%
3. Which of the following sentences about NAFLD is true?
 - a. It is a benign condition at no risk of evolution
 - b. It is a condition at high risk of evolution towards end-stage liver disease
 - c. It is the most frequent cause of dyspepsia
 - d. It is a hepatocyte fatty degeneration in patients with altered glucose or lipid metabolism
 - e. It never affects children

4. Which of the following conditions is often associated with NAFLD?
 - a. Type II diabetes
 - b. Arterial hypertension
 - c. Metabolic syndrome
 - d. Hyper/dyslipidemia
 - e. Coronary heart disease
5. Who among the following patients is more likely to have a NAFLD?
 - a. Subject with cholelithiasis
 - b. Diabetic subject
 - c. Obese subject
 - d. Patient with cardiovascular disease
 - e. Hypertensive subject
6. Which of the following criteria can be useful for NAFLD diagnosis?
 - a. Fatty liver at ultrasonography and high serum lipids levels
 - b. High serum triglyceride levels and elevation of serum transaminases
 - c. Elevation of at least one serum aminotransferase plus fatty liver at ultrasonography
 - d. Liver biopsy and histology
 - e. After exclusion of all other causes of liver steatosis
7. What is the best reason to ask for consultation?
 - a. Concomitant other liver disease
 - b. Association with metabolic syndrome
 - c. Presence of coronary heart disease
 - d. Young age at diagnosis
8. How do you approach a patient with NAFLD?
 - a. Diet and check again after one month
 - b. Search for associated conditions
 - c. Diet and new check after six months
 - d. Refer the patient to a specialist
9. Who is a good candidate for liver biopsy among the following NAFLD patients?
 - a. 19 year old severely obese subject (BMI >40 Kg/m²)
 - b. 40 year old female with high fasting glucose and hypertransaminasemia (2.5 UNV)
 - c. 50 year old diabetic patient with a history of 20 years of hypertransaminasemia
 - d. Young male subject (35 year old) with arterial hypertension
 - e. Never indicated
10. Who do you think is the most appropriate specialist to evaluate a NAFLD patient?
 - a. Gastroenterologist
 - b. Internist
 - c. Endocrinologist
 - d. Diabetologist
 - e. Lipidologist
11. Which is the best diet in a patient with NAFLD?
 - a. Hypocaloric diet
 - b. Low lipid content diet
 - c. Low carbohydrate content diet
 - d. High protein content diet
12. Which of the following medications has shown potential benefits in NAFLD patients?
 - a. Hepatoprotective agents
 - b. Diet regimen
 - c. Metformin and/or glitazones
 - d. Antioxidants
 - e. Lipid lowering agents
13. Which of the following drugs can precipitate or worsen a NAFLD condition?
 - a. ASA
 - b. Statins
 - c. Amiodarone
 - d. Paracetamol
 - e. Valproate

14. Are you interested in joining educational projects on NAFLD?
 - a. I am not interested
 - b. A little
 - c. Enough
 - d. I am very interested
 - e. I am very much interested

Table II. Questionnaire investigating daily practice about NAFLD.

1. In NAFLD patients, do you usually take into account extrahepatic associated conditions? If so, which one?
2. Do you search for NAFLD in patients at risk? If so, in which patients?
3. Do you consider the possibility that patients with a "simple" liver steatosis could have a NASH? If so, what do you do?
4. Do you believe that NAFLD can worsen the evolution of different chronic liver diseases? If so, what do you do?
5. Do you treat patients with NAFLD? If so, how?

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