Epidemiology of fatty liver: An update

Giorgio Bedogni, Valerio Nobili, Claudio Tiribelli

Epidemiology of fatty liver: An update

Giorgio Bedogni, Valerio Nobili, Claudio Tiribelli

WHAT IS FATTY LIVER?

A liver is said to be “fatty” when its hepatocytes contain more than 5% of triglycerides. The reference method for the diagnosis of FL is liver biopsy (LB), which is presently used to classify steatosis as light (5% to 33%), moderate (33% to 66%) or severe (> 66%). Although LB is the reference method for the diagnosis of FL, it is an imperfect gold-standard because of sampling error. More importantly, LB cannot be employed outside Liver Centers, and less invasive methods are needed to study the epidemiology of FL in the general population.

Liver ultrasonography (LUS) is the method most commonly employed to assess FL in the general population. Compared with LB, LUS has a sensitivity of...
NAFL(D) and AFL(D) cannot be distinguished at LB and their differentiation is based on the assessment of ethanol intake\(^{[20]}\). After exclusion of other causes of FL (mostly hepatitis B or hepatitis C virus infection and use of steatogenic drugs), the guidelines of the European Association for the Study of the Liver (EASL) suggest that NAFLD should be diagnosed when ethanol intake is less than or equal to 20 g/d in women and less than or equal to 30 g/d in men\(^{[26]}\). AGA guidelines suggest that NAFLD should be diagnosed when men consume less than or equal to 21 drinks per week and women consume less than or equal to 14 drinks per week\(^{[29]}\). Although the EASL and AGA cut-points are roughly equivalent, the former have the advantage of focusing on actual ethanol intake, possibly avoiding the problems associated with the choice of different “drink units”\(^{[30]}\).

The NAFL(D) vs AFL(D) categorization is vulnerable to many criticisms\(^{[27]}\). Besides the obvious loss of information\(^{[31]}\), the most important criticism is that such categorization hides the fact that obesity and alcohol interact in determining the prevalence and incidence of FL\(^{[25,33,34]}\). From a public health perspective, it is more useful to study the effect of alcohol intake on FL-related outcomes independently from other risk factors rather than dividing FL more or less arbitrarily into NAFL and AFL\(^{[10,17,28]}\). Another problem is that such a categorization assumes the use of an instrument accurate enough to detect small differences in ethanol intake. Even the 7-d weighted food record method that we employed in the Dionysos Nutrition and Liver study may not be accurate enough to detect such differences\(^{[32]}\).

**WHAT IS THE PREVALENCE OF FATTY LIVER?**

FL is the most common liver disease in Western countries, and NAFLD is the most common reason for altered liver enzymes in primary care\(^{[36]}\).

In the general population of the Dionysos Nutrition and Liver Study, 45% of individuals had any degree of FL at LUS\(^{[26]}\). Using a cut-point of 20 g/d for ethanol intake, 25% had NAFLD and 20% had AFL(D). A recent study performed in a large primary care practice has shown that nearly one in every three patients with persistently elevated alanine transaminase has NAFLD\(^{[35,36]}\).

Systematic reviews estimate that about 20%-30% of individuals in Western countries have NAFLD\(^{[36]}\) and similar figures are being increasingly provided for Eastern countries\(^{[37]}\). The prevalence of NAFLD increases with age, is highest in males between 40 and 65 years and is higher in Hispanics and lower in African-Americans\(^{[25,30,36]}\). The prevalence of NAFLD is increasing rapidly among children in parallel with the current epidemic of obesity\(^{[38]}\).

LUS data from the third edition of the National Health and Nutrition Examination Survey (NHANES III) (1988-1994) have recently been used to provide an estimate of the prevalence of FL in the general United States. LUS data from the third edition of the NHANES III showed that 16.1% of the population had abnormal liver enzymes, and 8.2% had steatosis of any degree. After exclusion of other causes of FL, 6.5% of the population had NAFLD. This estimate is lower than the prevalence of FL at LUS, which was estimated to be 14.2% by the same study. However, this estimate is likely to be biased by the use of LUS, which is less portable and more expensive than LUS. Although there are presently not enough data to draw definitive conclusions about the interchangeability of LUS and LB in pediatric age\(^{[13,14]}\).
WHAT IS THE RELATIONSHIP BETWEEN FATTY LIVER AND METABOLIC SYNDROME?

There is no doubt that NAFLD is more common among obese individuals and those with metabolic syndrome (MS)\(^{26,30}\). Because of this association, it has become common to state that NAFLD is the “hepatic component” of MS\(^{46}\). However, this hypothesis has not undergone formal testing until very recently\(^{47}\). A confirmatory factor analysis of NHANES III cross-sectional data has indeed shown that NAFLD is more likely to be a separate entity rather than an additional component of MS\(^{47}\). Even if NAFLD is not the “hepatic component” of MS, however, it remains to be tested whether MS and NAFLD contribute independently to ‘hard outcomes’ in the general population. This is important also in view of the ongoing controversy about the clinical relevance of the MS concept\(^{48,54}\).

Although NAFLD is most commonly associated with obesity, it is by no means uncommon in lean individuals. A recent analysis of NHANES III data has shown that the prevalence of NAFLD in lean individuals, defined as those with body mass index \(\leq 25\) kg/m\(^2\), is a quarter of that observed in overweight-obese individuals (7% vs 28%)\(^{49}\). Compared with its overweight-obese counterpart, ‘lean NAFLD’ is characterized by younger age, higher insulin sensitivity and lower frequency of MS\(^{53}\).

WHAT IS THE RELATIONSHIP BETWEEN FATTY LIVER AND CARDIOMETABOLIC DISEASE?

Much of the interest in NAFLD among researchers and clinicians outside the field of Hepatology stems from its association with cardiometabolic disease\(^{35,59}\).

In the last few years, an increasing number of cohort studies performed in the general population of Western and Eastern countries has shown that NAFLD, diagnosed by LUS or by surrogate markers such as FLI, is independently associated with incident T2DM\(^{46,50,51,52,54}\). The available evidence pointing to an association between NAFLD and incident cardiovascular disease (CVD) is presently of lower quality than that available for incident T2DM\(^{56}\). In a recent study performed in a tertiary CVD care center, NAFLD was associated with coronary artery disease but not with cardiovascular mortality\(^{54}\). Likewise, a recent analysis of NHANES III cohort data showed that NAFLD was associated with incident CVD but not with CVD mortality\(^{57}\).

The availability of long-term follow-up data in more or less representative samples of the general population will be central in coming years to improve our understanding of the NAFLD-CVD relationship.

REFERENCES


2. Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Ali-
Bedogni G et al. Epidemiology of fatty liver


27 Yilmaz Y. Review article: is non-alcoholic fatty liver disease a spectrum, or are steatosis and non-alcoholic steatohepatitis distinct conditions? *Aliment Pharmacol Ther* 2012; 36: 815-823 [PMID: 22966992]


