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Original Contribution

Prevalence of Nonalcoholic Fatty Liver Disease in the United States: The Third National Health and Nutrition Examination Survey, 1988–1994

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Previous estimates of the prevalence of nonalcoholic fatty liver disease (NAFLD) in the US population relied on measures of liver enzymes, potentially underestimating the burden of this disease. We used ultrasonography data from 12,454 adults who participated in the Third National Health and Nutrition Examination Survey, conducted in the United States from 1988 to 1994. We defined NAFLD as the presence of hepatic steatosis on ultrasonography in the absence of elevated alcohol consumption. In the US population, the rates of prevalence of hepatic steatosis and NAFLD were 21.4% and 19.0%, respectively, corresponding to estimates of 32.5 (95% confidence interval: 29.9, 35.0) million adults with hepatic steatosis and 28.8 (95% confidence interval: 26.6, 31.2) million adults with NAFLD nationwide. After adjustment for age, income, education, body mass index (weight (kg)/height $(m)^2$), and diabetes status, NAFLD was more common in Mexican Americans (24.1%) compared with non-Hispanic whites (17.8%) and non-Hispanic blacks (13.5%) ($P = 0.001$) and in men (20.2%) compared with women (15.8%) ($P < 0.001$). Hepatic steatosis and NAFLD were also independently associated with diabetes, with insulin resistance among people without diabetes, with dyslipidemia, and with obesity. Our results extend previous national estimates of the prevalence of NAFLD in the US population and highlight the burden of this disease. Men, Mexican Americans, and people with diabetes and obesity are the most affected groups.

ethnic variation; nonalcoholic fatty liver disease; population surveys; prevalence

Abbreviations: CI, confidence interval; HOMA-IR, homeostasis model assessment insulin resistance; NAFLD, nonalcoholic fatty liver disease; NHANES III, Third National Health and Nutrition Examination Survey.

In the United States, the burden of liver-related diseases is important. Over the last 2 decades, liver-related mortality ranked among the top 12 causes of death, and among adults aged 45–54 years, it has been repeatedly listed as the fourth leading cause of death (1, 2). Nonalcoholic fatty liver disease (NAFLD) is thought to be the most common chronic liver disease in the Western world (3–5). However, US estimates of the prevalence of NAFLD are lacking, and previous nationally representative studies have been limited by the use of surrogate markers of liver disease, namely liver enzymes, with estimates in the range of 3%–23% (6–9). Studies that have used more sensitive, specific, or direct methods have been limited by small sample size or by the use of convenience samples and report a range in the prevalence of NAFLD (19%–46%) (10, 11).

Although the "gold standard" for diagnosing and staging NAFLD is histology, abdominal unltrasonography allows its detection (4, 5). NAFLD was traditionally thought to be a benign condition; however, longitudinal studies have shown that it can progress to nonalcoholic steatohepatitis and fibrosis (12–14), leading to cirrhosis (15, 16). Also, there is increasing evidence suggesting that NAFLD may play a significant role in the strong association between obesity and the development of liver cancer (17, 18).

Large, population-based estimates of the prevalence of NAFLD as detected by ultrasonography are available for other Western and non-Western countries and show that its prevalence parallels that of obesity (11). For the United States, there are no representative data regarding the prevalence and epidemiology of this condition. These estimates

are key to assessing the magnitude of the disease and planning and projecting the health-care costs and the burden associated with liver disease. The Third National Health and Nutrition Examination Survey (NHANES III) was a large and representative survey of the noninstitutionalized US civilian population; it included gallbladder ultrasonography of all participants aged 20–74 years. Recently, we reevaluated these ultrasonography videotapes to assess the presence of hepatic steatosis.

By using these ultrasonography data, our aims were 1) to estimate the prevalence of any hepatic steatosis and NAFLD in the United States by key sociodemographic characteristics and 2) to examine metabolic, anthropometric, and laboratory correlates of hepatic steatosis and NAFLD.

MATERIALS AND METHODS

Study population

The NHANES III was conducted between 1988 and 1994 and is a cross-sectional national examination study conducted in the United States by the National Center for Health Statistics (Hyattsville, Maryland). The NHANES III was based on a complex multistage, stratified, clustered probability-sample design and comprised a representative sample of the US population living in households. The overall participation rate in the interview and examination was 78%. The complex NHANES III design and sampling can be used to generate estimates of health and disease in the general US population, incorporating adjustments for nonresponse. The NHANES III was approved by the institutional review board of the National Center for Health Statistics.

Data collection

Detailed descriptions of the NHANES III data collection are available elsewhere (19). Briefly, individuals received standardized interview questionnaires to provide sociodemographic data. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, and Mexican American. Individuals who did not identify themselves as belonging to 1 of these categories were not analyzed separately but were included in total estimates. Additional information included urbanization of the area and US geographic region of residence, smoking, alcohol use (a series of questions about the frequency per week and amount per day on a drinking day over the past 12 months), medical history (e.g., medication use, diagnosis of diabetes or hypertension, history of cardiovascular events), and physical activity. Adults were defined as sedentary if they answered "no" to all questions regarding engaging in any of the following activities over the last month: jogging/running, bicycling, swimming, aerobics, other dancing, calisthenics, garden/yard work, weight lifting, or other sports. Average alcohol consumption was estimated by multiplying the number of drinking days by the average number of drinks per day on a drinking day. "Never drinkers" were individuals who replied "no" to the following question: In your entire life, have you had at least 12 drinks of any kind of alcoholic beverage?

Body mass index was calculated as weight (kg)/height $(m)^2$. Gallbladder ultrasonography was performed by using a Toshiba Sonolayer V SSA-90A (Toshiba America Medical Systems, Inc., Tustin, California) with 3.75- and 5.0-MHz transducers (20).

Plasma glucose, serum insulin, serum total cholesterol, serum triglycerides, and serum high-density lipoprotein cholesterol levels were measured by using standardized methods. Low-density lipoprotein cholesterol levels were calculated from measured values of total cholesterol, triglycerides, and high-density lipoprotein cholesterol. Serum biochemistry analysis was performed by using the Hitachi 737 automated multichannel chemistry analyzer (Boehringer Mannheim Diagnostics, Inc., Indianapolis, Indiana). The following liver tests were assayed: asparatate aminotransferase, alanine aminotranferase, γ-glutamyl transferase, alkaline phosphatase, and total bilirubin. Presence of antibodies to hepatitis C was tested by using a second-generation enzyme immunoassay test (Abbott Laboratories, Ltd., Chicago, Illinois) and confirmed with the MATRIX assay (Abbott Laboratories, Ltd.). Antibodies to the hepatitis B core antigen were measured by using a solid-phase competitive immunoassay (Abbott Laboratories, Ltd.). Iron, total iron binding capacity, and ferritin were also measured. Serum transferrin saturation was calculated as serum iron (μg/dL) / serum total iron binding capacity (μg/dL) × 100 (21).

We defined diabetes on the basis of self-reported physician diagnosis, medication use, fasting plasma glucose ≥126 mg/dL, or 2-hour glucose tolerance test ≥200 mg/dL. Hypertension was defined on the basis of self-reported physician diagnosis, medication use, systolic blood pressure ≥140 mm Hg, or diastolic blood pressure ≥90 mm Hg. Finally, we defined hypercholesterolemia on the basis of self-reported physician diagnosis, medication use, or total cholesterol >240 mg/dL.

Among people without diabetes, we calculated insulin resistance by using the following homeostasis model assessment insulin resistance (HOMA-IR) formula: fasting serum insulin (μU/mL) × fasting plasma glucose (mmol/L) / 22.5. We used the adjusted insulin value for examinees. Elevated HOMA-IR was defined as >2.86, representing a level above the fourth quartile of HOMA-IR among people without diabetes (22).

Hepatic steatosis ultrasonography image assessment in the NHANES III

Between 2009 and 2010, hepatic steatosis examination was conducted to assess the presence of fat within the hepatic parenchyma. We retrieved and reviewed 13,856 gallbladder ultrasonography videotapes (96.6% of the original sample) that were originally obtained in the NHANES III between 1988 and 1994.

A more detailed description of the protocol can be found elsewhere (23). Briefly, the following information was recorded: 1) the presence of liver-to-kidney contrast (yes, no, or not assessed); 2) the degree of brightness of the liver parenchyma (none, intermediate, moderate, or severe); 3) the presence of posterior deep beam attenuation (yes, no, or not assessed); 4) the presence of echogenic walls in the small intrahepatic vessels (yes, no, or not assessed); and 5) the definition of the gallbladder walls (clear, intermediate,

obliterated, or not assessed). By using a standardized algorithm, we made an overall primary finding of hepatic steatosis on the basis of the presence or absence of each of the parameters listed above, and we graded the condition of the liver as normal, mild, moderate, or severe steatosis. Steatosis was also treated as a dichotomous variable (i.e., present (moderate or severe) or absent (normal-mild)). The rates of intra- and interrater reliability of the presence of hepatic steatosis were 0.77 (95% confidence interval (CI): 0.73, 0.82) and 0.70 (95% CI: 0.64, 0.76), respectively (23). The raters were unaware of the participants' health characteristics when grading the ultrasonography videotapes.

Definition of hepatic steatosis and NAFLD

We defined hepatic steatosis as the presence of moderate or severe hepatic steatosis by ultrasonography regardless of the presence of other liver disease markers (e.g., hepatitis C infection). Because there is no consensus definition in the literature, we defined NAFLD as the presence of hepatic steatosis in the absence of elevated alcohol consumption (≥1 drink/day for women and ≥2 drinks/day for men) as previously defined (24–26), or the use of zydovudine or didanosine, which are medications associated with the presence of hepatic steatosis (27).

Elevated levels of alanine aminotransferase or aspartate aminotransferase were defined on the basis of the upper limit of normal of the NHANES III laboratory values (alanine aminotransferase of >40 U/L for men and >31 U/L for women; aspartate aminotransferase of >37 U/L for men and >31 U/L for women) (21).

Statistical methods

Analyses included 12,454 NHANES III participants for whom we had complete information on all of the following: hepatic steatosis, racial/ethnic group, sex, age, body mass index, medication use, self-reported diabetes, alcohol consumption, viral hepatitis (B and C), transferrin levels, and levels of alanine aminotransferase and aspartate aminotransferase. No significant differences were observed between persons included in the analyses compared with those excluded. Thus, the analytical sample comprised 89.9% of all participants with hepatic steatosis data and 87.1% of all participants who underwent gallbladder ultrasonography during the 1988–1994 examinations. All analyses were performed by incorporating the sampling weights to obtain unbiased estimates from the complex NHANES III sampling design. The standard errors for all estimates were obtained by using the Taylor series (linearization), as recommended in the NHANES III (28). These methods allow findings to be generalized and to be considered nationally representative of the noninstitutionalized US population aged 20–74 years.

Age-adjusted prevalence estimates of NAFLD were computed by using direct standardization with age-based group proportions based on 2000 US Census data. Estimates of the affected population were obtained by multiplying the sex-race–specific prevalence estimates by the sex-race population totals (28). Given the high prevalence of NAFLD, we used the robust Poisson method to estimate the prevalence ratios of NAFLD by key metabolic characteristics while adjusting for confounders (29).

Although the main focus of the current analyses was NAFLD, we examined the prevalence and epidemiology of any hepatic steatosis and hepatic steatosis other than NAFLD, and the results are presented in detail in the Web tables available at http://aje.oxfordjournals.org/.

Analyses were conducted by using Stata, versions 10 and 11, software (StataCorp LP, College Station, Texas) and SAS software (SAS Institute, Inc., Cary, North Carolina). $P \leq 0.05$ was considered statistically significant. No corrections were made for multiple comparisons.

RESULTS

Prevalence of NAFLD

The age-adjusted prevalence of hepatic steatosis was 21.4% (95% CI: 19.7, 23.1), which corresponds to 32.5 (95% CI: 29.9, 35.0) million people in the United States. Ninety percent of these were considered to have NAFLD. The age-adjusted prevalence of NAFLD was 19% (95% CI: 17.5, 20.6), which corresponds to 28.8 (95% CI: 26.6, 31.2) million people in the United States.

As shown in Table 1, the prevalence of NAFLD was substantially higher among Mexican Americans compared with non-Hispanic whites and non-Hispanic blacks and among men compared with women. Across race and sex categories, the prevalence of NAFLD was lower among people aged 20–39 years compared with those aged ≥40 years. For every age category and for both men and women, Mexican Americans had a higher prevalence of NAFLD. The highest observed prevalence was 33% among Mexican-American men aged 40–59 years, followed by 29% among Mexican-American women of the same age group. As shown in Table 2, we also found a strong association between body mass index categories and the prevalence of NAFLD across racial/ethnic groups. A similar association was observed among people with high waist circumference (32.4% of whom had NAFLD compared with 9.7% of those with normal waist circumference).

To take into account differences in the prevalence of these risk factors across racial/ethnic groups, we calculated the adjusted prevalence of NAFLD for each racial/ethnic group. After adjustment for age, sex, education, income, diabetes, and body mass index, the 24.1% (95% CI: 20.8, 27.5) prevalence of NAFLD remained significantly higher for Mexican Americans (24.1%, 95% CI: 20.8%, 27.5%) compared with the 17.8% (95% CI: 16.1, 19.5) and 13.5% (95% CI: 11.3, 15.7) prevalence values for non-Hispanic whites and non-Hispanic blacks, respectively. Similarly, the estimated prevalence of NAFLD by sex adjusted for age, race, obesity status, diabetes, education, and income showed a significantly higher 20.2% (95% CI: 18.0, 22.5) prevalence among men compared with 15.8% (95% CI: 14.3, 17.2) prevalence among women ($P < 0.001$).

Association between metabolic risk factors and NAFLD

The adjusted prevalence ratios of NAFLD according to selected risk factors are shown in Table 3. In the age-, sex-,

Table 1. Prevalence of Nonalcoholic Fatty Liver Disease by Age, Race/Ethnicity, and Sex in the United States, NHANES III, 1988–1994

Sex by Age	Non-Hispanic White		Non-Hispanic Black		Mexican American		Total	
	Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI
Men								
<30 years	8.3	5.4, 12.7	10.9	7.5, 15.8	15.6	10.9, 21.8	9.9	7.4, 13.2
30–<40 years	15.9	12.5, 20.0	12.5	10.0, 15.6	25.7	21.6, 30.4	16.1	13.3, 19.4
40–<50 years	22.2	17.5, 27.7	17.1	12.7, 22.5	36.2	31.1, 41.6	22.3	18.2, 27.0
50–<60 years	28.0	21.5, 35.6	17.4	10.9, 26.6	41.4	31.3, 52.2	29.3	23.9, 35.4
≥60 years	28.1	24.4, 32.2	22.6	18.9, 26.8	33.4	27.6, 39.7	27.6	24.3, 31.3
Women								
<30 years	9.5	6.2, 14.2	12.0	8.7, 16.3	16.5	12.2, 22.0	10.6	7.9, 13.9
30–<40 years	11.1	8.4, 14.5	10.4	7.5, 14.1	23.2	18.6, 28.6	12.5	10.0, 15.6
40–<50 years	15.0	11.9, 18.7	14.3	9.8, 20.5	34.7	27.6, 42.6	16.1	13.4, 19.1
50–<60 years	20.5	16.7, 24.8	21.9	15.9, 29.4	35.7	25.6, 47.4	21.6	18.3, 25.3
≥60 years	25.7	22.3, 29.5	23.9	19.7, 28.8	34.4	28.8, 40.4	25.4	22.4, 28.6

Abbreviations: CI, confidence interval; NHANES III, Third National Health and Nutrition Examination Survey.

and race/ethnicity–adjusted analyses, those in the overweight and obese categories were significantly more likely to have NAFLD compared with individuals of normal weight. The prevalence ratios remained significant even after further adjustment for other metabolic abnormalities. Similarly, there was a strong and independent association between insulin resistance, with or without the presence of diabetes, and NAFLD. Additionally, sedentary individuals had a significantly higher prevalence of NAFLD independent of other risk factors. No significant interactions were found between age and sex, age and race/ethnicity, race/ethnicity and sex, or diabetes and body mass index.

Association between liver enzymes and NAFLD

The prevalence of elevated alanine aminotransferase was 6.0% (95% CI: 5.0, 7.2), and among these subjects, 41% (95% CI: 35.6, 45.9) had NAFLD. The prevalence of elevated aspartate aminotransferase was 5.6% (95% CI: 4.9,

Table 2. Age-Adjusted Prevalence of Nonalcoholic Fatty Liver Disease by Obesity Status, Race/Ethnicity, and Sex in the United States, NHANES III, 1988–1994

Sex by Obesity Status	Non-Hispanic White		Non-Hispanic Black		Mexican American		Total	
	Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI
Men								
Underweight[a]	10.1	3.1, 28.5	16.6	5.2, 41.8	3.6	0.4, 23.8	9.7	3.7, 22.9
Normal weight[b]	6.7	4.6, 9.6	8.2	5.7, 11.5	10.1	6.7, 14.8	7.5	5.6, 9.9
Overweight[c]	20.0	17.0, 23.3	13.0	10.2, 16.5	26.7	22.6, 31.3	19.9	17.4, 22.6
Obesity class 1[d]	38.8	32.4, 45.6	24.1	18.8, 30.3	48.6	40.3, 57.1	38.6	33.5, 44.0
Obesity class 2[e]	57.5	44.2, 69.7	43.9	34.0, 54.3	59.5	49.2, 69.0	56.6	46.5, 66.1
Women								
Underweight[a]	10.4	6.3, 16.7	16.7	8.4, 30.4	11.0	3.8, 28.2	13.6	8.2, 21.6
Normal weight[b]	6.5	4.7, 9.0	7.5	5.2, 10.5	12.0	8.8, 16.2	6.7	5.1, 8.6
Overweight[c]	17.3	14.6, 20.3	12.0	8.4, 16.8	20.9	16.8, 25.6	17.4	15.2, 19.8
Obesity class 1[d]	25.3	20.2, 31.2	15.8	11.0, 22.1	38.1	31.8, 44.9	24.7	20.8, 29.2
Obesity class 2[e]	47.5	40.7, 54.4	30.8	25.3, 37.0	52.2	41.6, 62.7	44.3	39.1, 49.6

Abbreviations: CI, confidence interval; NHANES III, Third National Health and Nutrition Examination Survey.
[a] Body mass index (weight (kg)/height $(m)^2$) of <18.5.
[b] Body mass index of 18.5–24.9.
[c] Body mass index of 25–29.9.
[d] Body mass index of 30–34.9.
[e] Body mass index of ≥35.

Table 3. Prevalence Ratios of Nonalcoholic Fatty Liver Disease in the United States, NHANES III, 1988–1994

Risk Factor	Age, Sex, and Race Adjusted		Model 1[a]		Model 2[b]	
	Prevalence Ratio	95% CI	Prevalence Ratio	95% CI	Prevalence Ratio	95% CI
BMI[c]						
<18.5	1.98	1.22, 3.21	2.01	1.23, 3.27	1.93	1.18, 3.14
18.5–24.9	1.00	Referent	1.00	Referent	1.00	Referent
25–29.9	2.34	1.96, 2.82	2.17	1.81, 2.60	2.12	1.77, 2.55
30–34.9	3.93	3.27, 4.73	3.31	2.74, 4.01	3.21	2.66, 3.86
≥35	6.62	5.51, 7.94	5.05	4.15, 6.14	4.67	3.84, 5.66
Diabetes/insulin resistance						
No diabetes/no insulin resistance	1.00	Referent	1.00	Referent	1.00	Referent
No diabetes/yes insulin resistance	2.54	2.23, 2.90	1.57	1.38, 1.80	1.49	1.31, 1.70
Yes diabetes	2.40	2.09, 2.76	1.60	1.39, 1.83	1.52	1.33, 1.74
Hypertension						
No	1.00	Referent	1.00	Referent	1.00	Referent
Yes	1.57	1.39, 1.78	1.07	0.95, 1.20	1.11	1.00, 1.25
Hypercholesterolemia						
No	1.00	Referent	1.00	Referent	1.00	Referent
Yes	1.26	1.11, 1.42	1.08	0.97, 1.21	1.09	0.97, 1.21
Sedentary						
No	1.00	Referent			1.00	Referent
Yes	1.31	1.16, 1.49			1.13	1.01, 1.27
Drinks per day	0.55	0.49, 0.62			0.62	0.56, 0.68

Abbreviations: BMI, body mass index; CI, confidence interval; NHANES III, Third National Health and Nutrition Examination Survey.

[a] Model 1 is adjusted for age, sex, race/ethnicity, and metabolic characteristics (BMI category, diabetes, hypertension, and hypercholesterolemia).

[b] Model 2 is adjusted for characteristics in Model 1, as well as lack of physical activity (sedentary) and number of alcoholic drinks per day.

[c] BMI is calculated as weight (kg)/height $(m)^2$.

6.4), and 33.8% (95% CI: 28.4, 39.7) of these subjects had NAFLD.

DISCUSSION

In this cross-sectional, nationally representative study, we found that hepatic steatosis detected by ultrasonography was present in almost 32.5 million adults or 21.4% of the US noninstitutionalized population aged 20–74 years between 1988 and 1994. The vast majority of the cases could be classified as NAFLD, with an overall prevalence of 19.0% (approximately 28.8 million people). Considerable variations in the prevalence of NAFLD by sex and by race/ethnicity were observed, with men and Mexican-American adults being disproportionally affected by all of these conditions and non-Hispanic blacks having a significantly lower burden of disease. In addition, we found that there were strong independent associations between diabetes or insulin resistance, dyslipidemia, and obesity with NAFLD.

Our findings regarding the magnitude of NAFLD and nonalcoholic steatohepatitis in the general US population have important implications. The rates of diabetes and obesity have been increasing steadily over the last 2 decades (30, 31), and on the basis of our results, we might expect a parallel increase in the number of people with NAFLD. In 2007–2008, the US Centers for Disease Control and Prevention reported that approximately 72.5 million adults in the United States were obese (32); based on our observed association between obesity and NAFLD, approximately 55 million adults currently might have NAFLD. Furthermore, because as many as 15% of people with NAFLD can progress to more advanced forms of liver disease such as fibrosis and cirrhosis, monitoring the prevalence of chronic liver disease would be prudent. Similarly, the association between NAFLD and hepatocellular carcinoma also highlights the relevance.

Over the last 2 decades there has been an increase in the number of people with end-stage liver disease requiring transplantation and in the incidence of hepatocellular

carcinoma (33). Others have suggested that these increases were due to chronic viral hepatitis. However, our data indicate that NAFLD is a more common condition, and its potential role as an underlying factor in these increases deserves attention, especially given recent supporting research (34, 35).

A number of prior studies have estimated the prevalence of NAFLD in the United States (7–9), including 1 study by our group (6). Most of these studies were based on the same national cross-sectional survey but were limited to examination of liver enzymes, which, in conjunction with other laboratory tests and self-reported data, allowed for an estimation of "explained" (e.g., elevated alcohol consumption, viral hepatitis) and "unexplained" elevation of liver enzymes in the general population, the latter of which was assumed to be NAFLD. Liver enzymes are surrogate markers of liver disease with known limited sensitivity and specificity (36, 37) and intraindividual variation (38). In fact, compared with the prevalence among the general population obtained in these studies, our study found a 3-fold higher prevalence of NAFLD depending on the definition used.

Another important population-based study based on the Dallas Heart Study (10) used proton magnetic resonance spectroscopy to quantify hepatic triglyceride content among 2,287 participants from Dallas County, Texas. The investigators defined hepatic steatosis as 5.5% or more hepatic fat as measured by proton magnetic resonance spectroscopy. By using that definition and tool, they found a prevalence of hepatic steatosis of 31%. There are several reasons why we may have found a lower prevalence. First, the Dallas Heart Study was conducted from 2000 to 2002 and included a representative sample of the population of Dallas County, which may not be representative of the US population; NHANES III occurred from 1988 to 1994 and included a nationally representative sample. Indeed, 43% of the study population in the Dallas Heart Study had obesity, whereas in the NHANES III population, the nationwide prevalence of obesity was 23.5%. Second, different imaging techniques were used. Our results are based on ultrasonography, which has a lower sensitivity for mild disease; therefore, our estimates may be conservative. More recently, Williams et al. (39) used ultrasonography to detect hepatic steatosis and found a 46% prevalence of NAFLD among a sample of 328 middle-aged adults who were seen at the Brooke Army Medical Center, including active duty military personnel, their dependents, and military retirees. Similar to the differences observed with the Dallas Heart Study, our results may differ from these because of geographical differences and time trends in the prevalence of risk factors, as well as a different population studied (NHANES does not include most military personnel).

We found significant differences in the prevalence of NAFLD by racial/ethnic groups and by sex independent of age, income, and metabolic and anthropometric characteristics. Although there is the potential of residual confounding by these factors, our findings are consistent with those of a number of previous studies and have important public health implications for the design and implementation of prevention and treatment strategies. A number of social, environmental, and genetic factors may account for this variation and merit future research.

Our study has several limitations. First, these data were collected more than 20 years ago; however, this is the only nationally representative US study with ultrasonography data available to determine the prevalence of this condition in the general population by key sociodemographic characteristics. In addition, the correlates of NAFLD found in our study should remain consistent. Although the overall sensitivity and specificity of ultrasonography compared with biopsy are approximately 85% and 94%, respectively (40), ultrasonography is relatively insensitive to smaller amounts of hepatic steatosis. In addition, ultrasonography cannot detect inflammation and fibrosis, which are hallmarks of more advanced stages of NAFLD. In the absence of a standard definition, we defined NAFLD by excluding people with hepatic steatosis in the presence of elevated alcohol intake or the use of antiretroviral medications, which were factors significantly associated with ultrasonography-detected hepatic steatosis. Our study was cross-sectional and therefore has some limitations and biases inherent to the design; we cannot establish causality or temporality between the risk factors studied and NAFLD. We describe the correlates of prevalent disease that may well be different from the correlates of incident cases. In addition, some selection bias may also be present because individuals with more severe forms of disease may have been less likely to participate in NHANES III; however, this bias would result in the underestimation of the observed association between the risk factors and NAFLD.

In conclusion, in 1988–1994 in the United States, the prevalence of NAFLD was already very high (19%). Furthermore, NAFLD disproportionally affects Mexican Americans, older adults, and people with diabetes and obesity. The aging of the population, along with the increasing prevalence of diabetes and obesity, is expected to contribute to an increase in the prevalence of these conditions and in the overall burden of liver disease in the United States. Randomized clinical trials have shown promising results by using lifestyle modification (41, 42), vitamin E and pioglitazone (43), and rosiglitazone (44), but there is no US Food and Drug Administration–approved drug for treating NAFLD. More research is needed to develop effective treatment options for people with NAFLD. In addition, given the prevalence of this condition, the development of improved assessment tools that can detect and stage NAFLD among the general population would be beneficial for future research.

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