Trends in Prevalence of Nonalcoholic Fatty Liver Disease in US Adults with Prediabetes

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INTRODUCTION

Prediabetes affects 84 million US adults, more than 50% of whom will develop diabetes in 15 years.[1] Once patients develop diabetes, up to 75% will have nonalcoholic fatty liver disease (NAFLD), and many of these will develop nonalcoholic steatohepatitis (NASH) and advanced fibrosis.[2] However, the burden of NAFLD and associated comorbidities in patients with prediabetes is less well understood. We aimed to estimate the population-based trends in prevalence of concurrent suspected NAFLD, advanced fibrosis and NASH cirrhosis in US adults with prediabetes.

METHODS

We conducted a cross-sectional, retrospective cohort analysis of the 2003–2014 National Health and Nutrition Examination Survey (NHANES). We included people aged ≥ 18 years who had a HbA1C from 5.7 to 6.4% or fasting plasma glucose from 100 to 125 mg/dL, or who were told they had prediabetes by a doctor but had never been diagnosed with diabetes. Patients with other causes of liver disease: viral hepatitis, excess alcohol consumption (> 1 drink/day for women, > 2 drinks/day for men); aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 500; pregnancy; or missing data were excluded. Suspected NAFLD was defined alternatively as hepatic steatosis index (HSI) > 36, fatty liver index (FLI) ≥ 60, either, or both.[3] NAFLD-associated advanced fibrosis was defined as BMI ≥ 25 kg/m^2, ALT > 40 U/L (men), or > 30 U/L (women) and either AST-to-platelet ratio index (APRI) > 1, fibrosis-4 (FIB-4) index > 2.67, or NAFLD fibrosis score (NFS) > 0.676.[4] Cirrhosis was defined as APRI > 2 and either ALT > 40 U/L (men) or > 30 U/L (women), alkaline phosphatase > 113 U/L, or total bilirubin > 1.3 mg/dL, and NASH cirrhosis as cirrhosis plus either obesity, insulin resistance, or metabolic syndrome.[4]

To improve precision, the prevalence of each condition was estimated in 4-year periods: 2003–2006, 2007–2010, and 2011–2014. We used logistic regression to examine trends, accounting for the complex survey design of NHANES.

RESULTS

Our final sample included 19,902 adults, of whom 7209 (36.2%) had prediabetes but only 4094 were included in the estimation of NASH cirrhosis due to missing data. Prevalence of prediabetes rose from 30.5 to 34.8% (p value = 0.009) while prevalence of concurrent prediabetes and suspected NAFLD remained stable (p value > 0.05) (Table 1). In prediabetic patients, prevalence of suspected NAFLD decreased significantly from 2003 to 2014 if suspected NAFLD was defined by FLI and by either FLI or HSI, but not by HSI and by both scores. Prevalence of NAFLD-associated advanced fibrosis did not change over time. Overall prevalence of NASH cirrhosis was 0.12% 95% CI: (-0.05)-0.28%. Translating to the general population, between 27 and 38 million US adults with prediabetes had suspected NAFLD (Fig. 1) and 420,000 patients had advanced fibrosis..

DISCUSSION

In this population-based study, we found that between 44 and 62% of US adults with prediabetes had concurrent suspected NAFLD, equivalent to 27–38 million patients, and similar to the numbers of prediabetic patients with hypertension or dyslipidemia. Our study appears to be the first to establish a population-based estimate of suspected NAFLD prevalence trends in prediabetic US adults. In Germany, the prevalence of NAFLD measured by localized proton magnetic resonance spectroscopy was 45–78%,[5] while in Korea, it was 60% based on ultrasound.[6]

The prevalence of prediabetes in the USA has been increasing for two decades, reaching 34% in 2015. Although intensive lifestyle modification and metformin have been shown to reduce progression to diabetes by 27% and 18%, respectively,[1] it is not known whether these interventions can affect liver function and prevent NAFLD progression. It is also not known to what extent these interventions are being used in clinical practice. Our findings that at least 27 million US adults have

Table 1 Prevalence (95% CI) of Suspected NAFLD and Advanced Fibrosis by Different Definitions Among US Adults, 2003–2014

	2003–2006	2007–2010	2011–2014	*p* value for trends
Total sample size	5783	7264	6855	
Prevalence of prediabetes (%)	30.5 [28.1–33.0]	37.2 [36.0–38.3]	34.8 [32.8–36.8]	0.009
Prevalence of concurrent prediabetes and suspected NAFLD in the general population (%)*				
HSI > 36	15.9 [14.0–17.7]	16.7 [15.4–18.0]	15.1 [13.8–16.5]	0.498
FLI ≥ 60	13.8 [12.1–15.5]	13.4 [12.3–14.4]	12.1 [10.7–13.5]	0.138
HSI > 36 or FLI ≥ 60	17.1 [15.3–19.0]	17.8 [16.6–19.1]	15.9 [14.3–17.4]	0.335
HSI > 36 and FLI ≥ 60	12.6 [10.9–14.3]	12.2 [11.1–13.3]	11.3 [10.1–12.5]	0.226
Prevalence of suspected NAFLD in the prediabetic population (%)†				
HSI > 36	61.0 [57.7–64.4]	56.5 [53.5–59.5]	56.9 [53.2–60.6]	0.112
FLI ≥ 60	53.2 [49.1–57.2]	45.4 [42.5–48.2]	45.7 [41.7–49.7]	0.013
HSI > 36 or FLI ≥ 60	65.5 [62.7–68.3]	60.4 [57.6–63.2]	59.8 [56.2–63.3]	0.015
HSI > 36 and FLI ≥ 60	48.7 [44.2–53.1]	41.5 [38.5–44.5]	42.8 [38.9–46.7]	0.059
Prevalence of NAFLD-associated advanced fibrosis in the prediabetic population (%)†				
Any score	0.67 [0.18–1.17]	0.54 [0.19–0.89]	0.77 [0.21–1.33]	0.779
APRI	0.38 [− 0.02–0.77]	0.36 [0.08–0.64]	0.29 [− 0.17–0.76]	0.79
FIB	0.27 [− 0.04–0.57]	0.18 [0.01–0.36]	0.38 [− 0.1–0.85]	0.678
NFS	0.18 [− 0.01–0.37]	0.41 [0.11–0.71]	0.48 [0.12–0.83]	0.139

*The prevalence was estimated among the general population
†The prevalence was estimated among the subset of prediabetic patients without any other causes of fatty liver. APRI, aspartate aminotransferase/platelet ratio index; CI, confidence interval; FLI, fatty liver index; HSI, hepatic steatosis index; NFS, nonalcoholic fatty liver disease fibrosis score; FIB-4, fibrosis-4 index

prediabetes and NAFLD suggests a coming epidemic of advanced liver complications if urgent prevention measures are not undertaken.

Our study is limited by the lack of biopsy and imaging data to confirm NAFLD-associated diagnosis. Nonetheless, we used two different noninvasive scores and different ways to define suspected NAFLD so as to provide conservative estimates, which were consistent with published studies. Addi-

tional limitations are the exclusion of normal BMI or liver enzyme in the definition of advanced fibrosis and limited sample size for the NASH cirrhosis estimate.

In conclusion, at least half of US adults with prediabetes had suspected NAFLD—a prevalence similar to that in diabetes. Pharmacological and nonpharmacological interventions that can address both diabetes development and NAFLD progression would be beneficial to the prediabetic population.
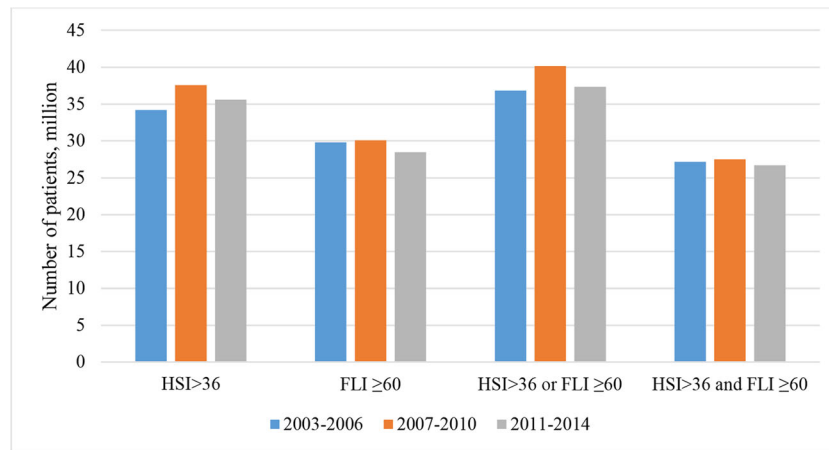

Figure 1 Population estimates of US adults with concurrent prediabetes and suspected NAFLD by different definitions of NAFLD, 2003–2014. FLI, fatty liver index; HSI, hepatic steatosis index; NAFLD, nonalcoholic fatty liver diseases.>

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