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Increasing Prevalence of Nonalcoholic Fatty Liver Disease Among United States Adolescents, 1988-1994 to 2007-2010

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Objective To assess recent trends in nonalcoholic fatty liver disease (NAFLD) prevalence among US adolescents.

Study design Cross-sectional data from 12 714 12-19 year olds (exclusions: chronic hepatitis, hepatotoxic medications) in the National Health and Examination Survey between 1988-1994 and 2007-2010 were used to estimate trends in suspected NAFLD, defined as overweight (body mass index ≥85th percentile) plus elevated alanine aminotransferase levels (boys >25.8 U/L; girls >22.1 U/L). Linear trends in prevalence and the independent effect of demographic indicators and adiposity on NAFLD risk were tested using regression models. Complex sampling methods and *P* values of <.05 were used to assess statistical significance.

Results Suspected NAFLD prevalence (SE) rose from 3.9% (0.5) in 1988-1994 to 10.7% (0.9) in 2007-2010 ($P < .0001$), with increases among all race/ethnic subgroups, males and females, and those obese (*P* trend ≤.0006 for all). Among those obese, the multivariate adjusted odds of suspected NAFLD were higher with increased age, body mass index, Mexican American race, and male sex; the adjusted odds in 2007-2010 were 2.0 times those in 1988-1994. In 2007-2010, 48.1% (3.7) of all obese males and 56.0% (3.5) of obese Mexican American males had suspected NAFLD.

Conclusion Prevalence of suspected NAFLD has more than doubled over the past 20 years and currently affects nearly 11% of adolescents and one-half of obese males. The rapid increase among those obese, independent of body mass index, suggests that other modifiable risk factors have influenced this trend. *(J Pediatr 2013;162:496-500)*.

Nonalcoholic fatty liver disease (NAFLD), is the most common form of liver disease in children.[1] A chronic, obesity associated condition, NAFLD can lead to cirrhosis and liver failure over time.[2] It is also an independent risk factor for cardiovascular disease and liver cancer.[3] Although previous studies have demonstrated differences in NAFLD prevalence rates across race/ethnicity,[4,5] sex,[6] age,[7] and weight status[8] subgroups, recent trends among adolescents and adolescent subgroups are not currently available. It is suspected that pediatric NAFLD prevalence has increased in parallel to the increasing trends in overweight and obesity over the past 3 decades[9] because of its association with obesity.

Previous reports have used varying approaches to estimate the prevalence of NAFLD.[10] Expert Committee guidelines recommend the use of serum transaminase levels[11] to screen for NAFLD though the specific cutpoints for defining elevation have not been specified. Alanine aminotransferase (ALT) levels at cutpoints of 30 U/L[7] and 40 U/L[6] have been commonly used but recent data suggests that such upper limits, which were defined using populations that included persons with subclinical liver disease, are too high.[12] Schwimmer et al recently evaluated the normal distribution of ALT levels in US adolescents and proposed a new set of cutpoints for screening for NAFLD based on the 95th percentile of this distribution, 25.8 U/L for boys and 22.1 U/L for girls.[6] A comparison of the results using these cutpoints to those obtained using liver ultrasound demonstrated that these sex-specific cutpoints were much more sensitive than the cutpoint of >30 (sensitivity 80% vs 36% for girls and 92% vs 32% for boys) and still highly specific (79% vs 92% for girls and 85% vs 96% for boys).[6]

The purpose of this study was to use national data, collected using the same or similar methods over the past 3 decades, to estimate current NAFLD prevalence rates among US adolescents and to determine if these rates have risen in line with the increase in obesity prevalence over this period.

Methods

We used national data from 12-19 year olds enrolled in the National Health and Nutrition Examination Survey 1988-1994 (NHANES III) or the continuous

ALT	Alanine aminotransferase
BMI	Body mass index
NAFLD	Nonalcoholic fatty liver disease
NHANES	National Health and Nutrition Examination Survey
NHANES III	National Health and Nutrition Examination Survey 1988-1994

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National Health and Nutrition Examination Survey (NHANES) between 1999 and 2010 (n = 14 918). NHANES is a cross-sectional survey of the US civilian, noninstitutionalized population designed to obtain nationally representative estimates on diet and health indicators. The sampling methodology is described elsewhere.[13] Subjects in the continuous NHANES were grouped into three 4-year periods, 1999-2002, 2003-2006, and 2007-2010 to provide sample sizes large enough to allow for subgroup analyses. Study subjects were excluded for known chronic liver disease (hepatitis B or C; n = 146), missing ALT data (n = 1476), missing data on covariates (n = 294), and treatment with hepatotoxic medications (n = 288; NHANES 1999-2010 only) for a final sample of 12 714. Institutional review board approval from the National Center for Health Statistics was obtained for this study. Signed, informed consent was obtained by National Center for Health Statistics from the parents/guardians of all participants and assent was obtained from all participants.[14]

Suspected NAFLD was defined as elevated ALT in an overweight or obese child (body mass index [BMI] for age and sex (BMI >85th percentile). Although NAFLD can occur in healthy weight children (particularly those approaching the 85th percentile BMI percentile), it is much more likely to occur in those overweight or obese.[7] Elevated ALT was defined using the sex-specific cutpoints recently proposed by Schwimmer et al[1] (>25.8 U/L for boys and >22.1 U/L for girls). For comparison purposes, national estimates were also obtained using ALT cutpoints of >30 U/L and >40 U/L. Serum ALT levels were determined using the enzymatic rate method.[15] We examined trends in suspected NAFLD by: weight category, including overweight (BMI 85th - <95th percentile), obese (BMI ≥95th percentile), and severely obese (BMI ≥99th percentile)[16]; sex; and race/ethnicity (non-Hispanic white, and non-Hispanic black, Mexican American, and other). High waist circumference, a measure of central adiposity, was defined as exceeding the 90th percentile for age, race, and sex as determined by Fernandez et al using data from adolescents participating in NHANES III.[17]

Statistical Analyses

Complex survey procedures in SAS 9.2 (SAS Institute, Cary, North Carolina) were used for all analyses. Variances were adjusted to account for the sampling methods used and weight factors were applied to estimates to make them representative of the US population. Frequency procedures were used to obtain unadjusted estimates of NAFLD prevalence at each time point studied and to assess trends nationally and by demographic and weight status subgroups. Linear trend testing was done using χ^2 tests for trend. Multivariate regression models controlling for age, sex, and race/ethnicity were used to examine the trends in NAFLD prevalence, elevated waist circumference, and BMI z-score among obese males and females. Finally, logistic regression models were used to assess the independent effects of known risk factors (age, sex, race/ethnicity, BMI, and waist circumference) on the odds of suspected NAFLD prevalence among a subsample including only obese adolescents and to compare this risk over time.

Results

A description of the weighted sample for each of the 4 study cycles is provided in Table I. There were no significant differences in age, sex, and percent overweight between NHANES III and the most recently released data cycles (2007-2010), but the proportion of adolescents who were Mexican American, obese, or severely obese did increase over the study period (*P* for trend <.0001 for all).

Trends in the unadjusted prevalence of suspected NAFLD, using each of the 3 cutpoints for elevated ALT, doubled among US adolescents between 1988-1994 and 2007-2010, rising from 0.8%-2.7% ($P < .0001$) using the most specific cutpoint of >40 U/L; from 2.3%-6.9% ($P < .0001$) using the more sensitive cutpoint of >30 U/L, and from 3.9%-10.7% using the recently defined sex-specific cutpoints of >25.8 U/L for boys and >22.1 U/L for girls ($P < .0001$) (Figure 1).

In stratified analyses, increasing trends in suspected NAFLD prevalence (defined using the sex-specific cutpoints) were observed among all race/ethnic subgroups, among both

Table I. Description of all adolescents (12-19 y) in sample, NHANES 1988-1994 to 2007-2010*,†

	1988-1994 N = 2748	1999-2002 N = 4004	2003-2006 N = 3824	2007-2010 N = 2138	*P* trend
Age, y	15.4 (0.1)	15.5 (0.1)	15.5 (0.1)	15.5 (0.1)	.43
Sex, % male	51.0 (1.8)	51.4 (1.0)	51.8 (1.1)	52.1 (1.2)	.61
Race/ethnicity					
White (non-Hispanic), %	67.1 (2.4)	58.9 (2.0)	63.0 (2.8)	58.9 (2.8)	.13
Black (non-Hispanic), %	14.7 (1.3)	14.2 (1.7)	15.2 (1.8)	14.2 (1.2)	.99
Mexican-American, %	8.6 (1.0)	10.9 (1.4)	11.6 (1.5)	13.6 (1.9)	.02
Other, %	9.5 (1.6)	16.1 (2.1)	10.2 (1.1)	13.3 (1.7)	.77
Overweight (BMI 85th - <95th percentile), %	15.9 (1.0)	15.8 (0.8)	17.6 (0.9)	17.7 (1.0)	.09
Obese (BMI ≥95th percentile), %	11.2 (1.0)	18.1 (0.8)	19.2 (1.3)	20.0 (1.1)	<.0001
Severe obesity (BMI ≥99th percentile), %	1.5 (0.4)	3.6 (0.5)	4.6 (0.6)	5.5 (0.9)	<.0001
BMI, z-score	0.38 (0.03)	0.54 (0.03)	0.60 (0.04)	0.64 (0.03)	<.0001
Waist circumference, cm	77.0 (0.5)	80.5 (0.4)	81.8 (0.5)	81.7 (0.4)	<.0001

*Weighted estimates.
†Figures presented are means (SE) unless indicated as %.