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The growing prevalence of nonalcoholic fatty liver disease (NAFLD), determined by fatty liver index, amongst young adults in the United States. A 20-year experience

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Abstract

Aim: The Global burden of nonalcoholic fatty liver disease (NAFLD) has significantly increased recently, with its prevalence mirroring increasing obesity and diabetes. However, population-specific evidence for young adults



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remains limited. Herein, we provide a 20-year trend analysis of NAFLD in young adults and examine factors associated with NAFLD and major adverse cardiovascular events (MACE) prevalence.

Methods: This study uses data from the United States National Health and Nutrition Examination Survey (NHANES) 1999-2018. Fatty liver was examined with the fatty liver index (FLI) and United States-FLI (US-FLI), and advanced fibrosis was examined with the fibrosis-4 index. Clustered multivariate logistic regression analysis on the year of study was applied to obtain odds ratios (OR) for the estimation of events.

Results: 13.31% (95%CI: 12.71% to 13.94%) of young adults had NAFLD. The prevalence increased from 9.98% in 1999 to 19.49% in 2018, with a statistically significant trend ($P < 0.001$). 9.52% and 5.29% of patients have clinically significant and advanced fibrosis, respectively. In multivariate analysis, diabetes (3.48, 95%CI: 2.37 to 5.11), hypertension (2.03, 95%CI: 1.62 to 2.55), elevated body mass index (1.22, 95%CI: 1.20 to 1.23, $P < 0.001$) significantly increases odds of NAFLD. The largest increase in odds was related to obesity (OR: 21.61, 95%CI: 16.95 to 27.55, $P < 0.001$). Young adults with NAFLD had a borderline non-significant increase in the prevalence of MACE compared to individuals without NAFLD (OR: 1.603, 95%CI: 0.949 to 2.708, $P = 0.078$).

Conclusion: The rising prevalence of NAFLD in young adults depicts the changing landscape of NAFLD and its association with a significant increase in MACE. The challenge of effective risk stratification and education of these individuals remains.

Keywords: NAFLD, prevalence, young Adults, epidemiology

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide, affecting approximately 25%-33% of the population^[1-4], and represents a spectrum of liver diseases that ranges from simple liver steatosis to non-alcoholic steatohepatitis (NASH). NASH is the more progressive form of the condition characterized by inflammation, hepatocyte ballooning and hepatocellular injury with or without fibrosis^[5]. The progression of NAFLD is associated with a range of liver-related sequelae such as cirrhosis, liver failure and hepatocellular carcinoma, with the leading cause of mortality being cardiovascular disease (CVD)^[6,7], which shares many remediable cardiometabolic risk factors encapsulated by metabolic syndrome, including obesity, atherogenic dyslipidemia, hypertension and hyperglycaemia^[8]. However, one should consider that there are circumstances in which this association does not apply^[9]; for example, isolated hepatic steatosis without further histological characteristics does not appear to influence stage-dependent CVD risk. Therefore, there is current dissonance on whether NAFLD confers additional independent CVD risk or whether an increase in CVD risk in NAFLD is due to associated CVD risk factors^[10]. Nevertheless, CVD mortality accounts for approximately 40% of all deaths in NAFLD patients^[11,12].

The prevalence of NAFLD in young adults has seen an alarming rise in NAFLD prevalence which mirrors the rising prevalence of obesity and type 2 diabetes (T2DM). Previous studies have shown NAFLD and NASH to have the highest prevalence among patients with DM, as opposed to other components of metabolic syndrome^[9,13]. Mrad *et al.* reported a rise in NAFLD prevalence in young adults in the United States from 9.6% in 1988-1994 to 24.0% in 2005-2010^[14]. Similarly, Lawlor *et al.* and Abeysekera *et al.* reported a rise in NAFLD prevalence from 2.5% to 20.7% among young adults from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort in the United Kingdom from a mean age of 17.9 to 24^[15,16]. An updated analysis of the epidemic of NAFLD in young adults has to be examined with more recent population data despite recent drastic increases in obesity and diabetes in young adults^[17]. Additionally, the relationship between cardiovascular health and NAFLD in young adults remains limited. Therefore, we

sought to examine the prevalence and risk factors associated with NAFLD and the risk of cardiovascular disease in the young adult population using patients recruited in the United States National Health and Nutrition Examination Survey (NHANES) between 1999-2018.

METHODS

The NHANES study examines aggregated health-related data from a clustered sampled national survey involving general and noninstitutionalised individuals in the United States between 1999-2018. The study involved participants undergoing comprehensive interviews, medical examinations, and laboratory assessments^[18]. Ethics approval by the Institutional Review Board was exempted due to the anonymous nature of the data made publicly available by the National Centre for Health Statistics (NCHS). Baseline characteristics such as but are not limited to age, gender, body mass index (BMI), ethnicity, income levels, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, total cholesterol, triglyceride, fasting blood glucose, glycohemoglobin, homeostatic model assessment for insulin resistance (HOMA-IR), platelet count, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and past medical history (diabetes, hypertension, obesity, smoking status) were collected. Information on longitudinal outcomes of patients, including major adverse cardiovascular events (MACE), was also collected.

The definition of NAFLD was adapted based on the American Association for the Study of Liver Disease (AASLD) guidelines for NAFLD^[19]. We defined NAFLD as the presence of steatosis in the absence of substantial alcohol use (≥ 3 drinks a day in men, ≥ 2 drinks a day in women). The presence of steatosis in NAFLD was quantified with either the fatty liver index (FLI) or the United States fatty liver index (US-FLI) with a cut-off of ≥ 60 ^[20] and ≥ 30 ^[21], respectively^[8,22]. Metabolic unhealthy patients were defined as individuals with fatty liver and concomitant type 2 diabetes and/or ≥ 2 metabolic risk abnormalities^[23]: (1) waist circumference ≥ 102 cm in men and 88 cm in women ($\geq 90/80$ cm in Asian men and women); (2) blood pressure $\geq 130/85$ mm Hg or receiving antihypertensives; (3) plasma triglycerides ≥ 2.3 mmol/L or receiving specific drug treatment; (4) plasma high-density lipoprotein < 1.00 mmol/L for men and < 1.30 mmol/L for women or specific drug treatment; (5) fasting blood glucose ≥ 100 mg/dL. Young adults were defined as individuals aged 18 to 30, while obesity status was defined as BMI ≥ 30.0 kg/m² for Caucasians and BMI ≥ 27.5 kg/m² for Asians^[24]. Diabetes was defined as glycohemoglobin $\geq 6.5\%$, fasting plasma glucose ≥ 7 mmol/L, self-reported diabetes or the use of anti-diabetic medications^[25]. Hypertension was defined as a systolic or diastolic blood pressure $\geq 130/85$ or the use of antihypertensive^[26]. Major adverse cardiovascular events (MACE) was an umbrella definition encompassing heart failure events, stroke, myocardial infarction and mortality^[27]. Advanced fibrosis was assessed by fibrosis-4 index (FIB-4), where a cut-off value of FIB < 1.3 ^[28] was defined as having a low risk of advanced fibrosis^[29]. A sensitivity analysis was then conducted to examine the prevalence of NAFLD with vibration-controlled transient elastography (VCTE). The NHANES 2017-2018 cycle was the only completed cycle with VCTE assessment of liver steatosis and fibrosis. A controlled attenuation parameter (CAP) score of ≥ 288 dB/m was selected for assessing liver steatosis^[30]. Clinically significant fibrosis (F2-4) was assessed with a liver stiffness (LSM) of ≥ 8.8 kPa^[31] and an LSM of ≥ 11.7 kPa^[32] for advanced fibrosis, respectively.

All statistical analysis was performed using STATA (16.1). Continuous variables were examined with Wilcoxon ranked sum test and Kruskal-Wallis analysis of variance, while binary variables were examined with chi-square test and Fisher's exact test where appropriate. Univariate and multivariate logistic regression analysis was used to obtain odds ratios (OR) for the estimation of common events and clinical interpretability in NAFLD and non-NAFLD young adults. A cluster analysis was also included based on the year of study to account for relevant heterogeneity introduced, using a cluster variable within multivariate

logistic regression that was constructed with important confounders that include age, gender, ethnicity, diabetes, smoking status and BMI. A trend analysis using the Cochran-Armitage test was also used to describe the relationship between NAFLD prevalence and the year of study.

RESULTS

Prevalence of NAFLD in young adults

In total, a total of 46,094 individuals were included in the analysis. A total of 27.09% (95%CI: 26.69% to 27.50%) had a diagnosis of NAFLD [Figure 1] and the prevalence of NAFLD by year groups is presented in Figure 2. A breakdown of age found a total population of 14,628 were between 18 to 30 years of age, 9228 were 31 to 40 years of age, 8907 were 41 to 50 years of age, 8329 were 51 to 60 years of age, 8517 were 61 to 70 years of age and 9422 were 70 years and older. The prevalence of NAFLD was 13.31% (95%CI: 12.71% to 13.94%), 24.96% (95%CI: 23.99% to 25.97%), 30.87% (95%CI: 29.81% to 31.96%), 35.40% (95%CI: 34.25% to 36.56%), 37.54% (95%CI: 36.39% to 38.70%) and 30.94% (95%CI: 29.83% to 32.07%) respectively in the age groups [Figure 3].

An analysis specific to young adults (18 to 30 years) based on the year of study on the proportion of NAFLD is presented in Figure 4. In total, 13.31% (95%CI: 12.71% to 13.94%) of young adults have NAFLD, of which 29.29% (25.66% to 33.20%) were classified as metabolically unhealthy. In young adults, the prevalence increased from 9.98% to 19.49% from 1999 to 2018. Trend analysis by the Cochran-Armitage test found a significant relationship between the year of study and the prevalence of NAFLD in young adults (Figure 4, $P < 0.001$). A sensitivity analysis was conducted to examine the prevalence of NAFLD based on VCTE only. However, VCTE was only available for the NHANES 2017-2018. A total of 1041 individuals were identified as young adults in the NHANES 2017-2018 cycle and the prevalence of NAFLD amongst these individuals was 18.16% (95%CI: 15.93 to 20.62) with a CAP score of 288 dB/m.

Most of the young adults were at low risk of advanced fibrosis ($FIB4 < 1.30$; 99.03%, 95%CI: 98.40% to 99.94%), with only a small proportion at intermediate-high risk of advanced fibrosis ($FIB4 \geq 1.30$, 0.07%, 95%CI: 0.06% to 1.60%). As FIB-4 is inaccurate in young adults, a sensitivity analysis was conducted to examine the prevalence of NAFLD based on liver stiffness from VCTE. The prevalence of clinically significant fibrosis (F2-4) and advanced fibrosis (F3-4) among young adults with NAFLD was 9.52% (95%CI: 6.06% to 14.65%) and 5.29% (95%CI: 2.86% to 9.59%), respectively.

Associated factors of NAFLD in young adults

A comparative analysis of the baseline characteristics between NAFLD and non-NAFLD is presented in Table 1. NAFLD individuals in young adults were found to be slightly older (24.70 vs. 22.87, $P < 0.001$) without any significant gender differences. Diabetes and hypertension were significantly associated with the presence of NAFLD (0.05 vs. 0.01, $P < 0.001$; 0.18 vs. 0.09, $P < 0.001$, respectively). Measures of lipids, including low-density lipoproteins, triglycerides and total cholesterol, were significantly higher in NAFLD individuals ($P < 0.001$). Similarly, the median liver enzyme levels were higher in NAFLD compared to non-NAFLD individuals ($P < 0.001$). The median BMI of young adults with NAFLD was significantly higher than non-NAFLD individuals (34.20 vs. 24.62, $P < 0.001$) and most of the young adults with NAFLD were found to be obese ($P < 0.001$).

There was a borderline non-statistical difference in ethnicity difference between NAFLD and non-NAFLD ($P = 0.051$). Multivariate logistic regression with a cluster variable on the year of study was used to examine baseline factors associated with NAFLD [Table 1]. Increasing age amongst young adults was a statistically significant factor resulting in NAFLD (OR: 1.11, 95%CI: 1.04 to 1.18, $P = 0.001$). Both BMI and waist

Table 1. Differences in baseline characteristics in young adults aged 18 to 30 with and without NAFLD

	NAFLD (n = 1562)	Non-NAFLD (n = 10,170)	P-value	Multivariate OR	P value
Age	24.70 (IQR: 22.00 to 28.00)	22.87 (IQR: 19.00 to 26.00)	< 0.001	1.11 (95%CI: 1.04 to 1.18)	0.001
Diabetes	0.05 (95%CI: 0.04 to 0.06)	0.01 (95%CI: 0.01 to 0.02)	< 0.001	3.48 (95%CI: 2.37 to 5.11)	< 0.001
BMI (kg/m ²)	34.20 (IQR: 31.09 to 38.70)	24.62 (IQR: 21.80 to 28.49)	< 0.001	1.22 (95%CI: 1.20 to 1.23)	< 0.001
Waist circumference (cm)	109.60 (IQR: 102.70 to 118.70)	85.20 (IQR: 95.40 to 77.30)	< 0.001	1.09 (95%CI: 1.08 to 1.10)	< 0.001
Obesity status					
Non-obese	0.19 (IQR: 0.18 to 0.20)	0.84 (IQR: 0.82 to 0.85)	< 0.001	Ref	
Obese	0.81 (IQR: 0.80 to 0.82)	0.16 (IQR: 0.15 to 0.18)		21.61 (95%CI: 16.95 to 27.55)	< 0.001
HTN	0.18 (95%CI: 0.16 to 0.20)	0.09 (95%CI: 0.08 to 0.09)	< 0.001	2.03 (95%CI: 1.62 to 2.55)	< 0.001
Gender					
			0.396		
Male	0.46 (95%CI: 0.44 to 0.49)	0.47 (95%CI: 0.46 to 0.48)		Ref	
Female	0.54 (95%CI: 0.51 to 0.56)	0.53 (95%CI: 0.52 to 0.54)		0.74 (95%CI: 0.58 to 0.94)	0.012
Platelet count	276.85 (IQR: 231.00 to 315.50)	260.05 (IQR: 216.00 to 296.00)	< 0.001	1.00 (95%CI: 0.99 to 1.01)	0.06
Glycohemoglobin (%)	5.37 (IQR: 5.10 to 5.50)	5.17 (IQR: 4.90 to 5.40)	< 0.001	1.47 (95%CI: 1.33 to 1.61)	< 0.001
HOMA	1.98 (IQR: 1.31 to 3.09)	4.24 (IQR: 2.75 to 6.52)	< 0.001	1.18 (95%CI: 1.12 to 1.23)	< 0.001
Fasting blood glucose (mg/dL)	96.00 (IQR: 89.00 to 103.00)	92.00 (IQR: 86.80 to 98.00)	< 0.001	1.01 (95%CI: 1.00 to 1.01)	0.001
Total cholesterol (mg/dL)	193.75 (IQR: 165.00 to 218.00)	175.41 (IQR: 149.00 to 196.00)	< 0.001	1.01 (95%CI: 1.01 to 1.02)	< 0.001
LDL (mg/dL)	114.13 (IQR: 91.00 to 135.00)	100.80 (IQR: 79.00 to 118.00)	< 0.001	1.01 (95%CI: 1.01 to 1.02)	< 0.001
HDL (mg/dL)	45.97 (IQR: 37.00 to 52.00)	53.94 (IQR: 44.00 to 62.00)	< 0.001	0.95 (95%CI: 0.93 to 0.97)	< 0.001
Triglycerides (mg/dL)	191.81 (IQR: 112.00 to 234.00)	107.87 (IQR: 59.00 to 129.00)	< 0.001	1.01 (95%CI: 1.01 to 1.02)	< 0.001
AST (IU/L)	22.00 (IQR: 18.00 to 28.00)	21.00 (IQR: 18.00 to 25.00)	< 0.001	1.01 (95%CI: 1.00 to 1.01)	0.024
ALT (IU/L)	24.00 (IQR: 17.00 to 37.00)	18.00 (IQR: 14.00 to 25.00)	< 0.001	1.01 (95%CI: 1.00 to 1.01)	< 0.001
Smoking status					
			< 0.001		
Non-smoker	0.73 (95%CI: 0.71 to 0.75)	0.66 (95%CI: 0.65 to 0.67)		Ref	
Former smoker	0.10 (95%CI: 0.09 to 0.12)	0.11 (95%CI: 0.11 to 0.12)		0.77 (95%CI: 0.61 to 0.97)	0.025
Current smoker	0.17 (95%CI: 0.15 to 0.19)	0.23 (95%CI: 0.22 to 0.24)		0.66 (95%CI: 0.56 to 0.76)	< 0.001
Ethnicity					
			0.051		
Mexican American	0.24 (95%CI: 0.22 to 0.27)	0.25 (95%CI: 0.24 to 0.26)		Ref	
Other Hispanic	0.07 (95%CI: 0.06 to 0.09)	0.08 (95%CI: 0.08 to 0.09)		0.94 (95%CI: 0.79 to 1.11)	0.452
Caucasian	0.33 (95%CI: 0.31 to 0.36)	0.35 (95%CI: 0.34 to 0.36)		1.00 (95%CI: 0.84 to 1.19)	0.977
African American	0.26 (95%CI: 0.24 to 0.28)	0.22 (95%CI: 0.21 to 0.23)		0.95 (95%CI: 0.76 to 1.19)	0.644
Others	0.09 (95%CI: 0.08 to 0.11)	0.09 (95%CI: 0.09 to 0.10)		1.36 (95%CI: 1.11 to 1.67)	0.003
Income levels					
			0.032		
Below 10,000	0.08 (95%CI: 0.07 to 0.10)	0.11 (95%CI: 0.10 to 0.12)		Ref	
10,000 to 24,999	0.25 (95%CI: 0.23 to 0.28)	0.26 (95%CI: 0.25 to 0.27)		1.23 (95%CI: 1.00 to 1.50)	0.045
25,000 to 44,999	0.28 (95%CI: 0.25 to 0.30)	0.26 (95%CI: 0.25 to 0.27)		1.25 (95%CI: 1.03 to 1.51)	0.023
45,000 to 74,999	0.24 (95%CI: 0.22 to 0.27)	0.23 (95%CI: 0.22 to 0.24)		1.21 (95%CI: 0.96 to 1.53)	0.114
Above 75,000	0.14 (95%CI: 0.13 to 0.16)	0.13 (95%CI: 0.13 to 0.15)		1.21 (95%CI: 1.00 to 1.46)	0.052

Bolded P-value ≤ 0.05 denotes statistical significance. NAFLD: Non-alcoholic fatty liver disease; OR: odds ratio; BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; HTN: hypertension; HOMA: homeostatic model assessment; AST: aspartate aminotransferase; ALT: alanine transaminase; IQR: interquartile range; 95%CI: 95% confidence interval.



Figure 1. Prevalence of NAFLD in the total and young adult population. NAFLD: Nonalcoholic fatty liver disease.

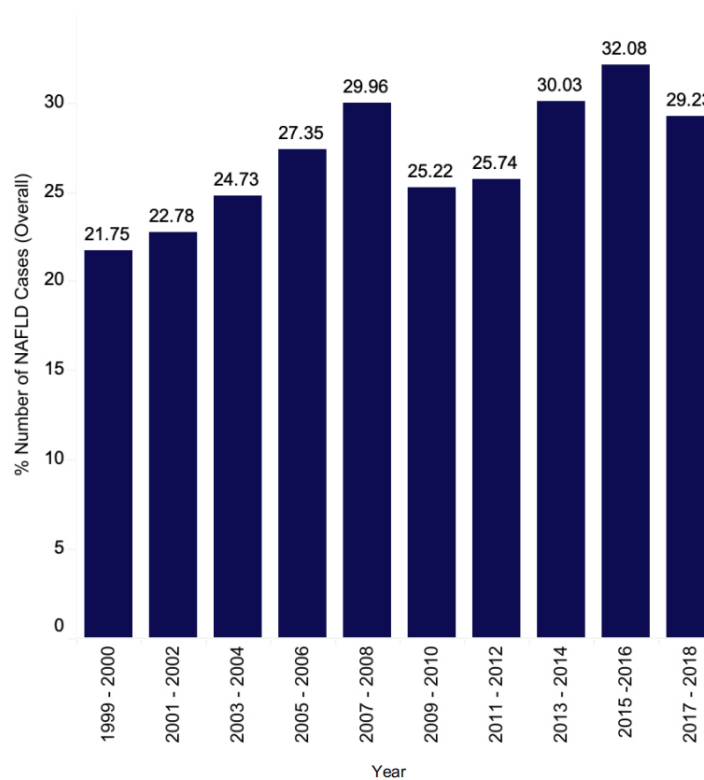


Figure 2. Prevalence of NAFLD by year of study. NAFLD: Nonalcoholic fatty liver disease.

circumference significantly increase the odds of NAFLD (1.22, 95%CI: 1.20 to 1.23, $P < 0.001$ and 1.09, 95%CI: 1.08 to 1.10, $P < 0.001$). Additionally, the female gender was less likely to be associated with NAFLD compared to the male gender (OR: 0.74, 95%CI: 0.58 to 0.94, $P = 0.012$) and lipid dysregulation significantly affected the odds of NAFLD [Table 1]. Interestingly, smoking history was associated with reduced odds of NAFLD as with higher income levels [Table 1]. The presence of diabetes affected only 5% of NAFLD individuals but resulted in a large increase in the odds of NAFLD (OR: 3.48, 95%CI: 2.37 to 5.11, $P < 0.001$). The largest increase in odds of NAFLD in young adults, however, was related to the presence of obesity (OR: 21.61, 95%CI: 16.95 to 27.55, $P < 0.001$)

MACE events in young adults with NAFLD

Young adults with NAFLD were then examined for an increased association between MACE and cardiovascular risk. MACE events were defined as any events of stroke, heart failure, myocardial infarction and cardiovascular mortality based on ICD. There were a total of 15 MACE events in 1416 NAFLD individuals and 41 MACE events in 6978 non-NAFLD individuals. An unadjusted clustered logistic regression found a significant increase in MACE events with young adults with NAFLD (OR: 1.81, 95%CI: 1.05 to 3.13, $P = 0.033$). A multivariate clustered logistic regression was then conducted, adjusting for age, gender, BMI, race, diabetes, and smoking status, and found a borderline non-significant increase in odds of

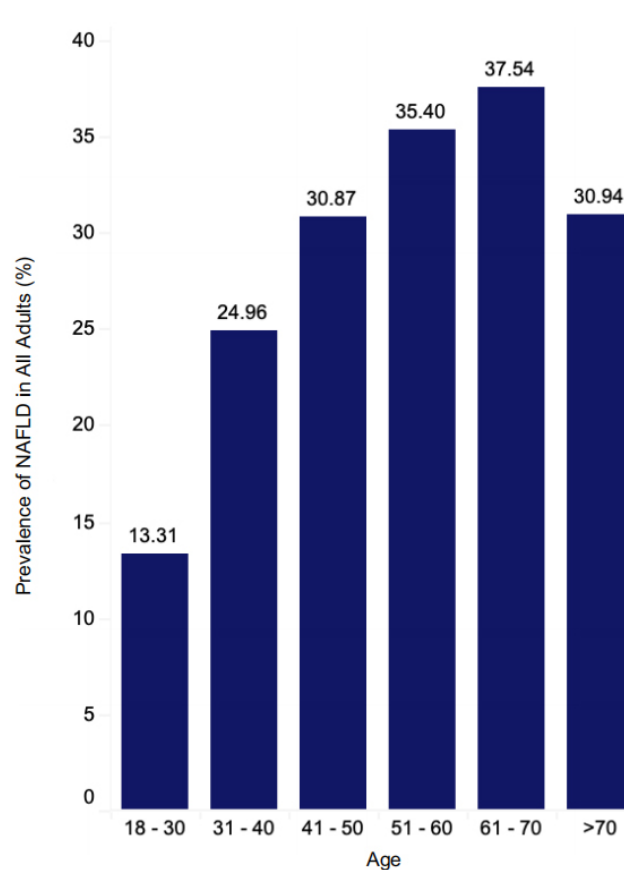


Figure 3. Prevalence of NAFLD by age group. NAFLD: Nonalcoholic fatty liver disease.

MACE events with NAFLD (OR: 1.59, 95%CI: 0.95 to 2.67, $P = 0.081$).

DISCUSSION

The epidemic of NAFLD has been well described in general adults and shown to significantly increase the risk of mortality^[33]. A lesser-known entity, however, lies in the prevalence of NAFLD in young adults who are often overlooked. In this study, we show that the overall prevalence of NAFLD in young adults (aged between 18 to 30) in this population database from the United States is estimated to be 13.31%. Within the young adult population, the proportion of NAFLD diagnoses doubled from 9.98% in 1999-2000 to 19.49% in 2017-2018 using FLI. Sensitivity analysis by VCTE with the NHANES 2017-2018 cycle similarly found that 18.16% (95%CI: 15.93 to 20.62) of young adults were affected by NAFLD. The findings are congruent with previous studies^[34,14] and emphasize the growing prevalence of NAFLD in young adults in the United States. However, the current study also shows the potential of NAFLD in young adults that may predispose the onset of MACE events (OR: 1.603, 95%CI: 0.949 to 2.708, $P = 0.078$), albeit with borderline non-significance.

There was an evident association between metabolic dysfunction where young adults with NAFLD had a higher prevalence of obesity, diabetes, hypertension, obesity, insulin resistance, dyslipidemia, and abnormal liver function test results. However, the largest increase in odds of NAFLD was found to be from obesity which had a 21 times increase in odds of NAFLD. Nevertheless, while an estimated 40%-45%^[8] of NAFLD are associated with diabetes and HTN, only 5% and 18% of young adults with NAFLD had HTN and diabetes. Significantly, only 29.29% of the young adult with NAFLD had metabolic dysfunction and the higher odds of NAFLD may relate to metabolically healthy obesity (MHO) status. MHO is a unique subtype

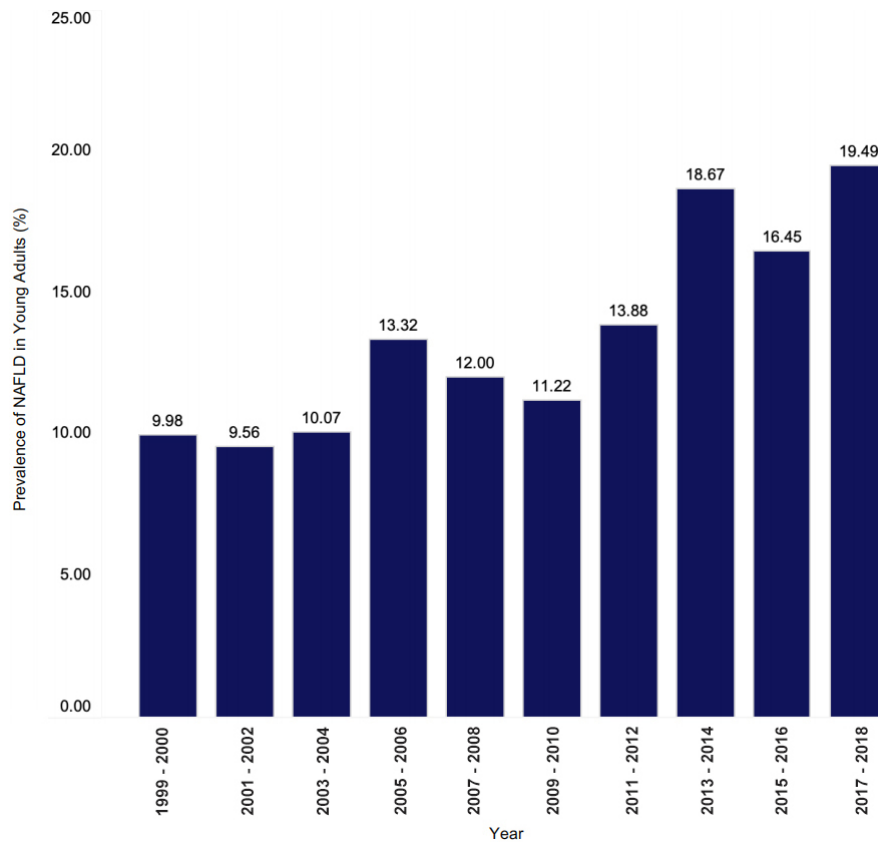


Figure 4. Prevalence of NAFLD in young adults by year of study. NAFLD: Nonalcoholic fatty liver disease.

of obesity more frequently found in younger individuals without significant metabolic dysfunction despite the presence of obesity^[35,36] which has been shown to predispose the risk of NAFLD^[37]. Additionally, the onset of NAFLD in young adults before evidence of other systemic dysregulation also alludes to the potential of fatty liver driving the development of other metabolic diseases. Only 5% and 18% of young adults with NAFLD have HTN or diabetes, respectively, which is a common commodity of NAFLD^[8,22], and NAFLD has been shown to longitudinally increase the risk of prediabetes and diabetes^[8]. This potentially alludes that the presence of hepatic fat may not be a bystander but rather a systemic driver of other metabolic disease^[38].

Female gender and smokers are associated with reduced odds of NAFLD diagnosis, and prior studies have attributed the protective effects of estrogen in pre-menopausal females to be protective towards NAFLD^[39]. Additionally, it was interesting to find that NAFLD individuals were less likely to be smokers. However, the negative association between NAFLD and smoking should be interpreted with caution as previous studies have reported contrasting associations between smoking and NAFLD^[40-42], and the effect of smoking may be too premature to manifest in young adults. Interestingly, lower income levels are also significantly associated with NAFLD diagnosis. This is in line with previous studies by Giammarino *et al.* and Golovaty *et al.* in predominantly older adults, which demonstrated the strong association between socioeconomic factors, including food insecurity and NAFLD in the United States^[43,44]. The availability, affordability and recognition of healthy food options and lifestyles need to be addressed in young adults, particularly those with lower income, to tackle the growing prevalence of NAFLD^[45].

Although cardiovascular events are rare in individuals below the age of 30, interestingly, there were a borderline 1.6 times odds of a non-significant increase in MACE events in young adults with NAFLD. A recently published long-term mortality data by Simon *et al.* showed that children and young adults with biopsy-proven NAFLD showed a significantly increased risk of long-term CVD-related mortality in NAFLD^[46]. However, risk stratification tools such as Framingham Heart Score, which are used to predict future MACE in older adults, perform poorly in individuals under 30^[47]. Therefore, there remains an unmet need to develop prognostication tools to identify individuals at risk of future cardiovascular disease in young adults with NAFLD.

Limitations

The current study has several limitations. NAFLD diagnosis was made through non-invasive means relying on FLI as a surrogate measure of steatosis but was deemed suitable considering the size of this population study. Additionally, FIB-4 score performs poorly in NAFLD patients under 35^[48]; therefore, the estimation of fibrosis may be inaccurate in the current study. A sensitivity analysis with VCTE instead showed that 5%-10% are likely to have clinically significant and advanced fibrosis. The population data was prevalent and did not collect the age of the first presentation of MACE among patients. Lastly, longitudinal outcomes of mortality were not assessed due to the significant duration of time needed for events to occur in young adults.

In conclusion, the prevalence of NAFLD is rising rapidly among the young adult population in the United States, with significant association with the obesity epidemic in young adults and the presence of which is associated with increased odds of MACE events. However, risk stratification of young adults with NAFLD remains challenging due to the lack of stratification tools in individuals below 35 and awareness of the disease can be significantly lower in this population.

DECLARATIONS

Authors' contributions

Conceptualisation and design: Li W, Ng CH, Muthiah M, Nouredin M

Acquisition of data: Quek J, Chan KE, Tan C, Zeng RW, Yong JN, Tay H, Tan DJH, Lim WH

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All authors approved the final version of the manuscript, including the authorship list and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Availability of data and materials

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Conflicts of interests

Sanyal A is President of Sanyal Biotechnology and has stock options in Genfit, Akarna, Tiziana, Indalo, Durect and Galmed. He has served as a consultant to Astra Zeneca, Nitto Denko, Enyo, Ardelyx, Conatus, Nimbus, Amarin, Salix, Tobira, Takeda, Janssen, Gilead, Terns, Birdrock, Merck, Valeant, Boehringer-

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Ethical approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The study was exempt from IRB review as no confidential patient information was involved.

Consent for publication

Not applicable.

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