Association between type 2 diabetes status and prevalence of liver steatosis and fibrosis among adults aged ≥ 40 years

Jun Chen¹, Piao Hu², Yanfei Wang³ and Zhongxin Zhu*¹

Abstract

Background: Type 2 diabetes mellitus (T2DM) and non-alcoholic fatty liver disease frequently coexist and share pathophysiological manifestations. This study aimed to explore the association between T2DM status and prevalence of liver steatosis and fibrosis, identified using the controlled attenuation parameter and liver stiffness measurement attained via liver ultrasound transient elastography.

Methods: This was a cross-sectional analysis of data collected in the National Health and Nutrition Examination Survey for 2017–2018. Multivariable logistic regression model was used to evaluate the association between T2DM and prevalence of liver steatosis and fibrosis. Subgroup analyses, stratified by sex age, race, and body mass index (BMI), were further performed.

Results: Of the 2,780 participants aged ≥ 40 years enrolled, 749 had T2DM, and 2,031 did not. After adjustment for potential confounders, T2DM was associated with a higher prevalence of liver steatosis (OR = 1.7, 95% CI, 1.3–2.1). This T2DM-related prevalence was higher among women (OR = 1.8, 95% CI, 1.3–2.5) and in the non-Hispanic Black (OR = 1.8, 95% CI, 1.1–3.0), other race (OR = 1.9, 95% CI, 1.2–3.0), and BMI < 25 kg/m² (OR = 2.0, 95% CI, 1.1–3.8) groups. T2DM was also associated with a significantly higher prevalence of fibrosis (OR = 2.0, 95% CI, 1.5–2.7), with this association being more prominent for the other race (OR = 2.9, 95% CI, 1.5–5.5) and BMI < 25 kg/m² (OR = 3.3, 95% CI: 1.3–8.8) groups.

Conclusions: Our findings indicated a positive association between T2DM status and prevalence of hepatic steatosis and fibrosis. This association was more prominent for individuals with a BMI < 25 kg/m² and was influenced by race-specific effects.

Keywords: Diabetes, Controlled attenuation parameter, Liver steatosis, Liver stiffness, Fibrosis

Background

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease and has become a major global health concern [1, 2]. In recent years, the prevalence of NAFLD has been rising progressively, along with type 2 diabetes mellitus (T2DM), which has reached epidemic levels [3]. T2DM is recognized as one of the strongest risk factors for the progression of NAFLD to non-alcoholic steatohepatitis, advanced fibrosis, or cirrhosis [4]. T2DM and NAFLD frequently coexist, with shared pathophysiological manifestations of excessive fat accumulation and insulin resistance [5].

The diagnosis of NAFLD is based on the detection of steatosis on liver biopsy and imaging techniques, after...
the exclusion of hepatic fatty infiltration and other causes of abnormal transaminase values via laboratory screening and medical history [6]. As a non-invasive imaging tool, liver ultrasound transient elastography (TE) provides excellent diagnostic accuracy for liver steatosis and advanced liver disease in adults [7]. The latest cycle of the National Health and Nutrition Examination Survey (NHANES) includes liver ultrasound TE for the diagnosis of liver steatosis and advanced liver disease based on the controlled attenuation parameter (CAP) and liver stiffness measurement (LSM). Herein, we explored the association between T2DM status and prevalence of liver steatosis and fibrosis, indicated by the CAP and LSM, among adults aged ≥ 40 years using the NHANES database.

**Methods**

**Study population**

This cross-sectional study used data from the NHANES database (2017–2018 cycle). The NHANES is a program designed to provide objective health data of the population of the United States. The methodology and data collection for the NHANES are freely available (http://www.cdc.gov/nchs/nhanes.htm) and have been fully described [8]. Among 3,882 adults aged ≥ 40 years whose data were available in the database, the following were excluded: 441 for whom serum glucose or glycohemoglobin (HbA1c) data were unavailable; 234 without CAP or LSM data; 375 due to the presence of hepatitis B surface antigen, hepatitis C antibody, or a history of significant alcohol consumption (men: > 30 g/day; women: > 20 g/day) [9], 26 aged < 30 years at the time of diabetes mellitus (DM) onset; and 26 without body mass index (BMI) data. We included 2,780 participants in the final analysis.

The National Center for Health Statistics Research Ethics Review Board approved the survey protocol and all participants provided written informed consent for data collection and the use of their information for research. Our study is compliant with the Guidelines for the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines [10].

**Study variables**

The exposure for our study is the T2DM status, defined according to the following criteria: participants being informed that they had DM by their doctor, age at time of DM diagnosis ≥ 30 years; and/or a HbA1c level ≥ 6.5% [11]. Outcomes on liver ultrasound TE were measured using a FibroScan® system (model 502, V2 Touch) and included CAP, with a value ≥ 274 dB/m indicative of liver steatosis [12], and LSM, with a median value ≥ 8 kPa indicative of significant fibrosis [13], provided by the liver ultrasound TE on a FibroScan® model 502 V2 Touch equipped with a medium or extra large probe. The following demographic and clinical variables were also collected as covariates in our analyses: age; sex; race; level of education; ratio of family income to poverty; level of moderate recreational activities; history of smoking ≥ 100 cigarettes; BMI; and blood urea nitrogen (BUN) levels, total cholesterol, uric acid, gamma-glutamyl transpeptidase (GGT), aspartic acid transferase, alanine amino transferase (ALT), alkaline phosphatase (ALP), and serum glucose.

**Statistical analysis**

All analyses were performed using statistical software R (version 3.4.3) and EmpowerStats (X&Y Solutions, Boston, MA), with a P-value < 0.05 considered significant. Multivariable logistic regression model was used to evaluate the association between T2DM status and prevalence of liver steatosis and fibrosis. Three statistical models were constructed: model 1, no adjustment for covariates; model 2, adjusted for age, sex, and race; and model 3, adjusted for all covariates presented in Table 1. Subgroup analyses, stratified by sex, age, race and, BMI were further performed.

**Results**

The characteristics of the study sample, according to T2DM status, are presented in Table 1. Of the 2,780 participants enrolled, 749 had a diagnosis of T2DM, with the other 2,031 classified in the non-DM group. Compared to the non-DM group, participants with T2DM were older, had a higher BMI and levels of ALP, ALT, GGT, uric acid, and BUN, had higher CAP and LSM values, a higher proportion of liver steatosis and significant fibrosis, and a lower level of total cholesterol.

**Association between T2DM status and CAP**

After adjustment for potential confounding factors, T2DM status was positively associated with CAP (β = 16.8, 95% CI, 11.8–21.8; Table 2). On subgroup analyses, this positive association was more prominent among women (β = 19.7, 95% CI, 12.6–26.7) than it was among men (β = 12.2, 95% CI, 4.9–19.4), and in the non-hispanic black (β = 19.5, 95% CI, 9.1–29.9), other race (β = 19.4, 95% CI, 10.2–28.5), and BMI < 25 kg/m² (β = 19.8, 95% CI, 8.7–31.0) groups.

**Association between T2DM status and risk of liver steatosis**

In the fully adjusted model (Table 3), T2DM status was positively associated with prevalence of liver steatosis (OR = 1.7, 95% CI, 1.3–2.1). On subgroup analyses, this positive association was more prominent among women (OR = 1.8, 95% CI, 1.3–2.5) than men (OR = 1.5, 95% CI:
Table 1  Characteristic of study sample with and without type 2 diabetes

| Characteristic                                | Non-diabetes (n = 2,031) | Type 2 diabetes (n = 749) | P value |
|-----------------------------------------------|--------------------------|---------------------------|---------|
| Age (years)                                   | 59.5 ± 11.8              | 64.3 ± 10.4               | < 0.001 |
| Sex (%)                                       |                          |                           | < 0.001 |
| Men                                           | 45.6                     | 53.5                      |         |
| Women                                         | 54.4                     | 46.5                      |         |
| Race (%)                                      |                          |                           | < 0.001 |
| Non-Hispanic White                            | 37.2                     | 29.9                      |         |
| Non-Hispanic Black                            | 21.9                     | 24.0                      |         |
| Mexican American                              | 11.9                     | 16.0                      |         |
| Other race                                    | 29.0                     | 30.0                      |         |
| Educational level (%)                         |                          |                           | < 0.001 |
| Less than high school                         | 19.9                     | 27.0                      |         |
| High school                                   | 24.0                     | 22.6                      |         |
| More than high school                         | 56.0                     | 50.5                      |         |
| Body mass index (kg/m²)                       | 29.3 ± 6.7               | 32.2 ± 7.3                | < 0.001 |
| Ratio of family income to poverty             | 2.7 ± 1.6                | 2.6 ± 1.6                 | 0.231   |
| Moderate recreational activities (%)          |                          |                           | < 0.001 |
| Yes                                           | 40.4                     | 31.9                      |         |
| No                                            | 59.6                     | 68.1                      |         |
| Smoked at least 100 cigarettes in life (%)    |                          |                           | 0.008   |
| Yes                                           | 41.9                     | 47.5                      |         |
| No                                            | 58.1                     | 52.5                      |         |
| Glycohemoglobin (%)                           | 5.6 ± 0.4                | 7.4 ± 1.5                 | < 0.001 |
| Serum glucose (mmol/L)                        | 5.3 ± 0.7                | 7.9 ± 3.5                 | < 0.001 |
| Alkaline phosphatase (U/L)                    | 80.7 ± 24.4              | 85.6 ± 30.9               | < 0.001 |
| Alanine amino transferase (IU/L)              | 20.9 ± 12.9              | 22.9 ± 15.8               | < 0.001 |
| Aspartic acid transferase (IU/L)              | 21.4 ± 9.0               | 21.8 ± 13.1               | 0.372   |
| Gamma-glutamyl transpeptidase (IU/L)          | 30.0 ± 37.8              | 37.5 ± 44.0               | < 0.001 |
| Serum uric acid (umol/L)                      | 323.5 ± 85.6             | 343.3 ± 94.7              | < 0.001 |
| Blood urea nitrogen (mmol/L)                  | 56.6 ± 2.0               | 64.0 ± 3.0                | < 0.001 |
| Total cholesterol (mmol/L)                    | 5.1 ± 1.0                | 4.6 ± 1.2                 | < 0.001 |
| Median controlled attenuation parameter (dB/m) | 264.5 ± 58.2             | 301.8 ± 59.0              | < 0.001 |
| Liver steatosis (%)                           |                          |                           | < 0.001 |
| Yes                                           | 43.8                     | 67.6                      |         |
| No                                            | 56.2                     | 32.4                      |         |
| Median liver stiffness (kpa)                  | 5.7 ± 5.1                | 7.6 ± 6.5                 | < 0.001 |
| Significant fibrosis (%)                      |                          |                           | < 0.001 |
| Yes                                           | 9.4                      | 25.4                      |         |
| No                                            | 90.6                     | 74.6                      |         |

Mean ± SD for continuous variables: P value was calculated by one-way ANOVA (normal distribution) and Kruskal–Wallis H (skewed distribution) test
% for categorical variables: P value was calculated by chi-square test

1.0–2.1), and in the non-Hispanic Black (OR = 1.8, 95% CI, 1.1–3.0), other race (OR = 1.9, 95% CI, 1.2–3.0), and BMI < 25 kg/m² (OR = 2.0, 95% CI, 1.1–3.8) groups.

**Association between T2DM status and LSM**

In the fully adjusted model, there was a positive association between T2DM status and LSM (β = 0.8, 95% CI, 0.2–1.3; Table 4). On subgroup analyses, this positive association was only identified among men (β = 0.9, 95% CI, 0.0–1.8) and in the 40–59 age (β = 1.0, 95% CI, 0.1–1.8), other race (β = 1.8, 95% CI, 0.8–2.9), and BMI ≥ 30 kg/m² (β = 1.0, 95% CI, 0.1–1.9) groups.
In the fully adjusted model, T2DM status and prevalence of significant fibrosis were positively correlated (OR = 2.0, 95% CI, 1.5–2.7) (Table 5). On subgroup analyses, this positive association was more prominent among individuals in the other race (OR = 2.9, 95% CI, 1.5–5.5) and BMI < 25 kg/m² (OR = 3.3, 95% CI, 1.3–8.8) groups.

### Table 2: Association between type 2 diabetes status and controlled attenuation parameter (dB/m)

|                          | Model 1 β (95% CI, P)                        | Model 2 β (95% CI, P)                        | Model 3 β (95% CI, P)                        |
|--------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 37.4 (32.5, 42.3) < 0.001                    | 39.1 (34.2, 44.1) < 0.001                    | 16.8 (11.8, 21.8) < 0.001                    |
| Stratified by sex        |                                             |                                             |                                             |
| Men (n = 1,328)          |                                             |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 31.3 (24.2, 38.5) < 0.001                    | 34.0 (26.7, 41.2) < 0.001                    | 12.2 (4.9, 19.4) 0.001                      |
| Women (n = 1,452)        |                                             |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 41.7 (35.0, 48.4) < 0.001                    | 44.2 (37.4, 51.0) < 0.001                    | 19.7 (12.6, 26.7) < 0.001                    |
| Stratified by age        |                                             |                                             |                                             |
| 40–59 age group (n = 1,240) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 47.2 (38.6, 55.7) < 0.001                    | 47.1 (38.6, 55.7) < 0.001                    | 19.1 (10.4, 27.8) < 0.001                    |
| 60–80 age group (n = 1,540) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 35.0 (29.0, 41.1) < 0.001                    | 34.3 (28.3, 40.3) < 0.001                    | 15.4 (9.0, 21.7) < 0.001                     |
| Stratified by race       |                                             |                                             |                                             |
| Non-Hispanic White (n = 979) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 41.6 (32.7, 50.5) < 0.001                    | 43.5 (34.6, 52.4) < 0.001                    | 13.2 (3.9, 22.5) 0.005                      |
| Non-Hispanic Black (n = 624) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 34.6 (24.5, 44.7) < 0.001                    | 37.5 (27.4, 47.6) < 0.001                    | 19.5 (9.1, 29.9) < 0.001                     |
| Mexican American (n = 362) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 29.9 (17.6, 42.2) < 0.001                    | 29.9 (16.9, 42.8) < 0.001                    | 12.0 (-1.1, 25.2) 0.074                     |
| Other race (n = 815)     |                                             |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 39.1 (30.5, 47.8) < 0.001                    | 38.0 (29.1, 47.0) < 0.001                    | 19.4 (10.2, 28.5) < 0.001                    |
| Stratified by body mass index (BMI) |                                   |                                             |                                             |
| BMI < 25 (kg/m²) (n = 632) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 32.4 (22.2, 42.6) < 0.001                    | 29.3 (19.0, 39.5) < 0.001                    | 19.8 (8.7, 31.0) < 0.001                     |
| BMI ≥ 25, < 30 (kg/m²) (n = 951) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 27.5 (19.7, 35.4) < 0.001                    | 24.3 (16.2, 32.4) < 0.001                    | 14.4 (5.0, 23.8) 0.003                      |
| BMI ≥ 30 (kg/m²) (n = 1,197) |                                   |                                             |                                             |
| Non-diabetes             | Reference                                   | Reference                                   | Reference                                   |
| Type 2 diabetes          | 25.0 (18.5, 31.6) < 0.001                    | 27.2 (20.7, 33.7) < 0.001                    | 15.9 (8.7, 23.0) < 0.001                     |

Model 1: no covariates were adjusted
Model 2: age, sex, race were adjusted
Model 3: age, sex, race, educational level, body mass index, ratio of family income to poverty, moderate recreational activities, smoked at least 100 cigarettes in life, blood urea nitrogen, total cholesterol, serum uric acid, alkaline phosphatase, alanine amino transferase, aspartic acid transferase, Gamma-glutamyl transpeptidase, and serum glucose were adjusted

### Association between T2DM status and risk of significant fibrosis

In the fully adjusted model, T2DM status and prevalence of significant fibrosis were positively correlated (OR = 2.0, 95% CI, 1.5–2.7) (Table 5). On subgroup analyses, this positive association was more prominent among individuals in the other race (OR = 2.9, 95% CI, 1.5–5.5) and BMI < 25 kg/m² (OR = 3.3, 95% CI, 1.3–8.8) groups.
Table 3 Association between type 2 diabetes status and prevalence of liver steatosis

|                      | Model 1 OR (95% CI, P) | Model 2 OR (95% CI, P) | Model 3 OR (95% CI, P) |
|----------------------|------------------------|------------------------|------------------------|
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.7 (2.2, 3.2) < 0.001 | 2.9 (2.4, 3.4) < 0.001 | 1.7 (1.3, 2.1) < 0.001 |
| **Stratified by sex**|                        |                        |                        |
| **Men (n = 1,328)**  |                        |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.3 (1.8, 3.0) < 0.001 | 2.5 (2.0, 3.3) < 0.001 | 1.5 (1.0, 2.1) 0.033   |
| **Women (n = 1,452)**|                        |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 3.0 (2.3, 3.9) < 0.001 | 3.2 (2.5, 4.1) < 0.001 | 1.8 (1.3, 2.5) 0.001   |
| **Stratified by age**|                        |                        |                        |
| **40–59 age group (n = 1,240)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 3.4 (2.4, 4.7) < 0.001 | 3.4 (2.5, 4.8) < 0.001 | 1.4 (0.9, 2.2) 0.190   |
| **60–80 age group (n = 1,540)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.6 (2.1, 3.2) < 0.001 | 2.6 (2.1, 3.3) < 0.001 | 1.8 (1.3, 2.4) < 0.001 |
| **Stratified by race**|                        |                        |                        |
| **Non-Hispanic White (n = 979)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.9 (2.1, 4.0) < 0.001 | 3.0 (2.2, 4.2) < 0.001 | 1.2 (0.8, 1.9) 0.414   |
| **Non-Hispanic Black (n = 624)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.4 (1.7, 3.4) < 0.001 | 2.6 (1.8, 3.8) < 0.001 | 1.8 (1.1, 3.0) 0.014   |
| **Mexican American (n = 362)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.6 (1.6, 4.2) < 0.001 | 2.6 (1.5, 4.3) < 0.001 | 1.7 (0.9, 3.4) 0.129   |
| **Other race (n = 815)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.9 (2.1, 4.0) < 0.001 | 2.9 (2.1, 4.1) < 0.001 | 1.9 (1.2, 3.0) 0.003   |
| **Stratified by body mass index (BMI)** | |                        |                        |
| **BMI < 25 (kg/m²) (n = 632)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 3.0 (1.9, 4.8) < 0.001 | 2.6 (1.6, 4.3) < 0.001 | 2.0 (1.1, 3.8) 0.023   |
| **BMI ≥ 25, < 30 (kg/m²) (n = 951)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.2 (1.6, 2.9) < 0.001 | 2.0 (1.5, 2.8) < 0.001 | 1.5 (1.0, 2.2) 0.074   |
| **BMI ≥ 30 (kg/m²) (n = 1,197)** | |                        |                        |
| **Non-diabetes**     | Reference              | Reference              | Reference              |
| **Type 2 diabetes**  | 2.0 (1.5, 2.6) < 0.001 | 2.1 (1.6, 2.9) < 0.001 | 1.6 (1.1, 2.2) 0.012   |

Model 1: no covariates were adjusted
Model 2: age, sex, race were adjusted
Model 3: age, sex, race, educational level, body mass index, ratio of family income to poverty, moderate recreational activities, smoked at least 100 cigarettes in life, blood urea nitrogen, total cholesterol, serum uric acid, alkaline phosphatase, alanine amino transferase, aspartic acid transferase, Gamma-glutamyl transpeptidase, and serum glucose were adjusted

Discussion
In this study, we evaluated the association between T2DM status and prevalence of liver steatosis and fibrosis among adults aged ≥ 40 years, and found that T2DM was associated with a significantly higher prevalence of liver steatosis, with this association being more prominent among women and the non-Hispanic Black, other race, and BMI < 25 kg/m² groups. T2DM also
positively correlated with the prevalence of significant fibrosis, which was more prominent in the other race and BMI < 25 kg/m² groups.

| Model 1 β (95% CI, P) | Model 2 β (95% CI, P) | Model 3 β (95% CI, P) |
|-----------------------|-----------------------|-----------------------|
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 1.9 (1.4, 2.3) < 0.001| 1.8 (1.4, 2.3) < 0.001| 0.8 (0.2, 1.3) 0.006 |
| **Stratified by sex** |                       |                       |                       |
| **Men (n = 1,328)**   |                       |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 1.9 (1.2, 2.7) < 0.001| 2.0 (1.2, 2.8) < 0.001| 0.9 (0.0, 1.8) 0.046 |
| **Women (n = 1,452)** |                       |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 1.7 (1.2, 2.3) < 0.001| 1.7 (1.1, 2.2) < 0.001| 0.4 (-0.2, 1.1) 0.173|
| **Stratified by age** |                       |                       |                       |
| **40–59 age group (n = 1,240)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 2.6 (1.9, 3.3) < 0.001| 2.5 (1.8, 3.3) < 0.001| 1.0 (0.1, 1.8) 0.027 |
| **60–80 age group (n = 1,540)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 1.5 (0.9, 2.1) < 0.001| 1.5 (0.9, 2.1) < 0.001| 0.7 (-0.0, 1.4) 0.058|
| **Stratified by race** |                       |                       |                       |
| **Non-Hispanic White (n = 979)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 2.2 (1.3, 3.0) < 0.001| 2.1 (1.3, 2.9) < 0.001| 0.2 (-0.7, 1.2) 0.631|
| **Non-Hispanic Black (n = 624)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 0.7 (-0.3, 1.8) 0.170 | 0.7 (-0.3, 1.8) 0.176 | 0.0 (-1.2, 1.2) 0.980 |
| **Mexican American (n = 362)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 2.1 (1.3, 2.8) < 0.001| 1.8 (1.0, 2.7) < 0.001| 0.7 (-0.2, 1.6) 0.108|
| **Other race (n = 815)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 2.5 (1.6, 3.4) < 0.001| 2.4 (1.5, 3.3) < 0.001| 1.8 (0.8, 2.9) < 0.001|
| **Stratified by body mass index (BMI)** | |                       |                       |
| **BMI < 25 (kg/m²) (n = 632)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 0.9 (0.3, 1.5) 0.003  | 0.9 (0.2, 1.5) 0.006  | 0.5 (-0.2, 1.2) 0.130|
| **BMI ≥ 25, < 30 (kg/m²) (n = 951)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 1.1 (0.4, 1.9) 0.004  | 0.7 (-0.1, 1.5) 0.076 | 0.6 (-0.4, 1.6) 0.226|
| **BMI ≥ 30 (kg/m²) (n = 1,197)** | |                       |                       |
| **Non- diabetes**     | Reference             | Reference             | Reference             |
| **Type 2 diabetes**   | 2.0 (1.2, 2.8) < 0.001| 2.0 (1.2, 2.8) < 0.001| 1.0 (0.1, 1.9) 0.032 |

Model 1: no covariates were adjusted
Model 2: age, sex, race were adjusted
Model 3: age, sex, race, educational level, body mass index, ratio of family income to poverty, moderate recreational activities, smoked at least 100 cigarettes in life, blood urea nitrogen, total cholesterol, serum uric acid, alkaline phosphatase, alanine amino transferase, aspartic acid transferase, Gamma-glutamyl transpeptidase, and serum glucose were adjusted

The bidirectional and mutual relationship between T2DM and NAFLD has been highlighted by epidemiological studies, with NAFLD increasing the risk of T2DM incidence, and T2DM increasing the risk of
NAFLD incidence and progression [14]. A recent meta-analysis showed that the pooled prevalence of NAFLD among adults with T2DM was around 60%, with this prevalence varying by age and by BMI [15]. Compared to non-diabetes patients, those with combined NAFLD and T2DM have a higher risk of NAFLD progression [16]. A previous NHANES study (NHANES III) revealed that diabetes was associated with all-cause

| Model 1 OR (95% CI, P) | Model 2 OR (95% CI, P) | Model 3 OR (95% CI, P) |
|------------------------|------------------------|------------------------|
| Non-diabetes Reference | Reference Reference Reference |
| Type 2 diabetes 3.3 (2.6, 4.1) < 0.001 | 3.3 (2.6, 4.2) < 0.001 2.0 (1.5, 2.7) < 0.001 |
| Stratified by sex Men (n = 1,328) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 2.9 (2.2, 4.0) < 0.001 | 3.1 (2.3, 4.3) < 0.001 1.8 (1.2, 2.8) 0.004 |
| Women (n = 1,452) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 3.6 (2.6, 5.0) < 0.001 | 3.6 (2.5, 5.0) < 0.001 2.0 (1.3, 3.1) 0.003 |
| Stratified by age 40–59 age group (n = 1,240) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 4.6 (3.2, 6.6) < 0.001 | 4.5 (3.1, 6.5) < 0.001 2.3 (1.4, 3.9) 0.002 |
| 60–80 age group (n = 1,540) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 2.7 (2.1, 3.7) < 0.001 | 2.7 (2.0, 3.7) < 0.001 2.0 (1.4, 2.9) < 0.001 |
| Stratified by race Non-Hispanic White (n = 979) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 3.5 (2.4, 5.2) < 0.001 | 3.5 (2.4, 5.3) < 0.001 2.0 (1.2, 3.4) 0.011 |
| Non-Hispanic Black (n = 624) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 1.9 (1.2, 2.9) 0.008 | 1.9 (1.2, 3.0) 0.006 1.7 (1.0, 3.1) 0.067 |
| Mexican American (n = 362) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 3.0 (1.7, 5.3) < 0.001 | 3.0 (1.6, 5.5) < 0.001 1.6 (0.7, 3.7) 0.228 |
| Other race (n = 815) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 5.5 (3.5, 8.6) < 0.001 | 5.5 (3.4, 8.8) < 0.001 2.9 (1.5, 5.5) 0.001 |
| Stratified by body mass index (BMI) Non-diabetes Reference Reference Reference |
| BMI < 25 (kg/m²) (n = 632) Type 2 diabetes 2.4 (1.2, 4.7) 0.013 | 2.3 (1.1, 4.8) 0.021 3.3 (1.3, 8.8) 0.015 |
| BMI ≥ 25, < 30 (kg/m²) (n = 951) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 2.7 (1.6, 4.4) < 0.001 | 2.2 (1.3, 3.8) 0.003 1.5 (0.7, 3.1) 0.257 |
| BMI ≥ 30 (kg/m²) (n = 1,197) Non-diabetes Reference Reference Reference |
| Type 2 diabetes 2.9 (2.2, 3.9) < 0.001 | 2.9 (2.2, 3.9) < 0.001 2.3 (1.6, 3.3) 0.001 |

Model 1: no covariates were adjusted
Model 2: age, sex, race were adjusted
Model 3: age, sex, race, educational level, body mass index, ratio of family income to poverty, moderate recreational activities, smoked at least 100 cigarettes in life, blood urea nitrogen, total cholesterol, serum uric acid, alkaline phosphatase, alanine amino transferase, aspartic acid transferase, Gamma-glutamyl transpeptidase, and serum glucose were adjusted
and cardiovascular mortality among individuals with NAFLD [17].

Among the non-invasive tests for NAFLD, TE is the most widely used for the assessment of liver fibrosis [18]. A higher prevalence of advanced fibrosis assessed via TE was observed among patients with T2DM [19–22]. The results of a recent NHANES study reported high rates of hepatic steatosis and fibrosis, diagnosed by CAP and LSM, among patients with T2DM, but with race-dependent differences [23]. Similarly, in our study, the association between T2DM status and CAP or LSM was prominent in some races, but not in others, including a non-significant association among Mexican–American individuals.

The common pathophysiological mechanisms shared by NAFLD and T2DM include a series of metabolic changes; in particular, changes in the white adipose tissue may play a central role in the initiation of both NAFLD and T2DM [24]. In 2020, an international panel of experts from 22 countries proposed the novel term “metabolic dysfunction-associated fatty liver disease” to replace NAFLD, which further emphasizes the strong association between T2DM and NAFLD [25]. NAFLD and T2DM not only have almost the same risk factors, but also have synergistic effects on each other’s disease progression and complications. Therefore, routine screening for T2DM among individuals with NAFLD and lifestyle changes, including diet modifications and physical activity, are recommended for the prevention and management of both T2DM and NAFLD.

Our study had some limitations. First, as this was a cross-sectional study, no causality could be established. Second, we excluded participants with age of DM onset of < 30 years of age to minimize the number of participants with T1DM, as previously described [26, 27], as the NHANES database does not differentiate diabetes by type. Third, the values of CAP defining hepatic steatosis and LSM defining significant fibrosis are both inconsistent among different studies using NAHENS 2017–2018 database [13, 28, 29]. Thus, the sensitivity and specificity of TE test may vary depending on the cut-off values. Fourth, differences in measurements depending on the probe used in FibroScan have been demonstrated in previous reports [30, 31]. However, the elastography exams were performed by trained and certified technicians, according to the manufacturer guidelines [32]. Last, self-reported confounders may be susceptible to individual biases. This source of bias was minimized by the utilization of the NHANES data, which is collected by trained personnel through established procedures.

Conclusion
In conclusion, our findings indicate that T2DM is positively associated with prevalence of hepatic steatosis and fibrosis. This association was more prominent for individuals with a BMI < 25 kg/m² and was influenced by race-specific effects. Routine screening for T2DM among individuals with NAFLD may contribute to the prevention and the management of both T2DM and NAFLD.

Abbreviations
NAFLD: Non-alcoholic fatty liver disease; T2DM: Type 2 diabetes mellitus; TE: Transient elastography; NHANES: National Health and Nutrition Examination Survey; CAP: Controlled attenuation parameter; LSM: Liver stiffness measurement; HbA1c: Glycohemoglobin; BMI: Body mass index; DM: Diabetes mellitus; BUN: Blood urea nitrogen; GGT: Gamma-glutamyl transpeptidase; ALT: Alanine amino transferase; ALP: Alkaline phosphatase.

Acknowledgements
The authors appreciate the time and effort given by participants during the data collection phase of the NHANES project.

Author contributions
JC, PH, and YFW contributed to data collection, analysis and writing of the manuscript. ZXZ contributed to study design and editing of the manuscript. The author(s) read and approved the final manuscript.

Funding
This study received no funding.

Availability of data and materials
The datasets generated and analysed during the current study are available in the NHANES website (http://www.cdc.gov/nchs/nhanes.htm).

Declarations
Ethics approval and consent to participate
The ethics review board of the National Center for Health Statistics approved all NHANES protocols and written informed consents were obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Department of Endocrinology, The First People’s Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou 311200, Zhejiang, China. 2 Department of Infectious Diseases, The First People’s Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou 311200, Zhejiang, China. 3 Department of Medical Oncology, The First People’s Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou 311200, Zhejiang, China. 4 Clinical Research Center, The First People’s Hospital of Xiaoshan District, Xiaoshan Affiliated Hospital of Wenzhou Medical University, Hangzhou 311200, Zhejiang, China.

Received: 8 March 2022   Accepted: 10 May 2022
Published online: 13 May 2022
References

1. Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, Bugianesi E. Global burden of NASH and NAFLD: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018;15(11):1–20.

2. Mitra S, De A, Chowdhury A. Epidemiology of non-alcoholic and alcoholic fatty liver diseases. Transl Gastroenterol Hepatol. 2020;5:16.

3. Lee CH, Lui D, Lam K. Non-alcoholic fatty liver disease and type 2 diabetes - An Update. J Diabetes Invest. 2022.

4. Targher G, Corey KE, Byrne CD, Roden M. The complex link between NAFLD and type 2 diabetes mellitus - mechanisms and treatments. Nat Rev Gastroenterol Hepatol. 2021;18(9):599–612.

5. Golabi P, Paik JM, Mqoqhtani S, Younossi Y, Tuncer G, Younossi ZM. Burden of non-alcoholic fatty liver disease in Asia, the Middle East and North Africa. Data from Global Burden of Disease 2009–2019. J Hepatol. 2021;75(4):795–809.

6. Yu EL, Golshan S, Harlow KE, Angeles JE, Durelle J, Goyal NP, Newton KP, Angeles JE, Durelle J, Goyal NP, Newton KP. Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease in Children With Obesity. J Pediatr. 2019;207:64–70.

7. Ramírez-Véllez R, García-Hermoso A, Correa-Rodríguez M, Izquierdo M: Defining values for controlled attenuation parameter and liver stiffness in youth without liver disease. Pediatr Res 2021.

8. Johnson CL, Paulose-Ram R, Ogden CL, Carroll MD, Kruszon-Moran D, Defining values for controlled attenuation parameter and liver stiffness in youth without liver disease. Pediatr Res 2021.

9. Lai LL, Wang TY, et al. Prevalence of Nonalcoholic Fatty Liver Disease in Children and Adolescents. J Pediatr. 2015;166(4):396–402.

10. Schröder B, Kahl S, Roden M. Non-alcoholic fatty liver disease in type 2 diabetes - A specific entity? Liver Int. 2021;41(Suppl 1):105–11.

11. Elamin MM, Elamin HA, slice M, et al. Predicting early-stage fibrosis in populations with non-alcoholic fatty liver disease. Liver Int. 2020;40(10):2655–63.

12. Sayes CM, Sfarti C, Trifan A, Zenovia S, Cuciureanu T, Nastasa R, Huiban J. Non-alcoholic fatty liver disease in children: clinical and histological features and treatment outcomes. Pediatr Gastroenterol Hepatol. 2021;100(6):2231–8.

13. Vermeulen MJ, Brouwer H, Raat JJ, et al. Advanced liver disease in children with type 2 diabetes mellitus and high prevalence of non-alcoholic fatty liver disease. J Pediatr. 2019;207:64–70.

14. Dickerson MT, Anstee QM, McPherson S. Non-alcoholic fatty liver disease: a clinical review. J Pediatr. 2019;207:64–70.

15. Oeda S, Takahashi H, Imajo K, Seko Y, Ogawa Y, Moriguchi M, Yoneda M, Anzai K, Aisihuma S, Kage M, et al. Accuracy of liver stiffness measurement and controlled attenuation parameter using FibroScan(®) M/XL probes to diagnose liver fibrosis and steatosis in patients with nonalcoholic fatty liver disease: a multicenter prospective study. J Gastroenterol. 2020;55(4):428–40.

16. Chan WK, Nik Mustapha NR, Wong GL, Wong VW, Mahadeva S. Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2019;156(6):1717–30.

17. Liu X, Shen H, Chen M, Zhao J. Clinical Relevance of Vitamins and Carotenoids With Liver Steatosis and Fibrosis Detected by Transient Elastography in Adults. Front Nutr. 2021;8:760985.

18. Muzica CA, Starni C, Tielan A, Zinova S, Cuiucerianu T, Nastasa R, Hubian L, Cobbold JP, Deeks JJ, Paradis V, et al. Accuracy of FibroScan Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2019;156(6):1717–30.

19. Guha IN, Cobbold JP, Deeks JJ, Paradis V, et al. Accuracy of FibroScan Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. J Pediatr. 2019;207:64–70.

20. Lee CH, Lui D, Lam K. Non-alcoholic fatty liver disease and type 2 diabetes - A specific entity? Liver Int. 2021;41(Suppl 1):105–11.

21. Elamin MM, Elamin HA, slice M, et al. Predicting early-stage fibrosis in populations with non-alcoholic fatty liver disease. Liver Int. 2020;40(10):2655–63.

22. Lai LL, Wang TY, et al. Prevalence of Nonalcoholic Fatty Liver Disease in Children and Adolescents. J Pediatr. 2015;166(4):396–402.

23. Sayes CM, Sfarti C, Trifan A, Zenovia S, Cuciureanu T, Nastasa R, Huiban J. Non-alcoholic fatty liver disease in children: clinical and histological features and treatment outcomes. Pediatr Gastroenterol Hepatol. 2021;100(6):2231–8.

24. Dickerson MT, Anstee QM, McPherson S. Non-alcoholic fatty liver disease: a clinical review. J Pediatr. 2019;207:64–70.

25. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, Zelber-Sagi S, Wai-Sun Wong V, Dufour JF, Schattenberg JM, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020;73(1):202–9.

26. Andary R, Fan W, Wong ND. Control of Cardiovascular Risk Factors Among US Adults With Type 2 Diabetes With and Without Cardiovascular Disease. Am J Cardiol. 2019;124(4):522–7.

27. Yao X, Xu X, Jin F, Zhu Z. The Correlation of Type 2 Diabetes Status With Bone Mineral Density in Middle-Aged Adults. Diab Metab Syndr Obesity Targets Ther. 2020;13:3269–76.

28. Gangireddy VSR, Pikerton C, Xiang J, Tinajero R, Ashcraft AM. Hepatic Steatosis and Steatosis in Metabolic Syndrome. J Obesity Metab Syndr. 2022;31(1):61–9.

29. Heredia NJ, Zhang X, Balakrishnan M, Hwang JP. Thir AP: Association of lifestyle behaviors with non-alcoholic fatty liver disease and advanced fibrosis detected by transient elastography among Hispanic/Latinos adults in the U.S. Ethnicity Health 2022. p. 1–14.

30. Oeda S, Takahashi H, Imajo K, Seko Y, Ogawa Y, Moriguchi M, Yoneda M, Anzai K, Aishuma S, Kage M, et al. Accuracy of liver stiffness measurement and controlled attenuation parameter using FibroScan(®) M/XL probes to diagnose liver fibrosis and steatosis in patients with nonalcoholic fatty liver disease: a multicenter prospective study. J Gastroenterol. 2020;55(4):428–40.

31. Chan WK, Nik Mustapha NR, Wong GL, Wong VW, Mahadeva S. Controlled Attenuation Parameter and Liver Stiffness Measurement in Assessing Steatosis and Fibrosis in Patients With Nonalcoholic Fatty Liver Disease. Gastroenterology. 2019;156(6):1717–30.

32. Younossi ZM, Golabi P, de Avila P, Paik JM, Srishord M, Fukui N, Qiu Y, Burns J, Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions