Association Between Hypertension and the Prevalence of Liver Steatosis and Fibrosis

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Abstract

Background

Hypertension (HTN) and non-alcoholic fatty liver disease (NAFLD) usually occur together and have some common pathophysiological symptoms. In this study, we determined the relationship between HTN status and the rates of liver steatosis and fibrosis based on the liver stiffness measurement and controlled attenuation parameter obtained by performing liver transient ultrasound elastography (TUE).

Methods

To perform this cross-sectional study, data were obtained from the National Health and Nutrition Examination Survey for 2017-March 2020 Pre-pandemic cycle. The relationship between HTN and the rates of liver steatosis and fibrosis was analyzed by constructing a multivariate logistic regression model. We also conducted subgroup analyses based on the age, gender, ethnicity, and body mass index (BMI) of the patients.

Results

In total, 4,837 participants were recruited, including 2,375 participants with HTN and 2,462 participants without HTN. After adjusting possible confounders, HTN was positively related to the liver steatosis rate (OR = 1.4, 95% CI: 1.1–1.8). Such HTN-associated incidences were higher among males (OR = 1.6, 95% CI: 1.1–2.3), non-Hispanic African American individuals (OR = 1.9, 95% CI: 1.1–3.5), and participants with BMI ≥ 25 < 30 kg/m^2 (OR = 1.7, 95% CI: 1.1–2.5). Additionally, HTN was positively associated with the fibrosis rate (OR = 2.0, 95% CI: 1.3–3.0), especially among females (OR = 2.6, 95% CI: 1.3–5.1), among individuals who were 40–59 years old (OR = 2.3, 95% CI: 1.1–4.6), 60–80 years old (OR = 2.2, 95% CI: 1.2–4.1), non-Hispanic Caucasian (OR = 3.0, 95% CI: 1.6–5.9), among those with BMI ≥ 25 < 30 kg/m^2 (OR = 3.0, 95% CI: 1.1–8.1), and those with BMI ≥ 30 kg/m^2 (OR = 2.0, 95% CI: 1.2–3.3).

Conclusions

The results of this study showed that HTN status was positively associated with liver steatosis and fibrosis rates, especially for subjects with BMI ≥ 25 kg/m^2. The relationship was also affected by the ethnicity of the participants.

Background

Non-alcoholic fatty liver disease (NAFLD) is a frequently occurring chronic hepatopathy and an important global health issue[1, 2]. It occurs as a consequence of metabolic syndrome (MetS). The incidence of

NAFLD and hypertension (HTN) has reached epidemic levels[3]. Some systemic diseases, inflammatory disorders, alcoholism, and infection affect the liver and the heart. NAFLD represents the hepatic manifestation of metabolic disorders, which independently affects the occurrence of cardiovascular diseases (CVDs)[4]. HTN frequently accompanies NAFLD, which affects about 40% of the population. NAFLD might increase the risk of developing CVDs[5].

Non-alcoholic fatty liver disease (NAFLD) is usually diagnosed after liver steatosis is discovered based on liver biopsy, histological analysis, and imaging examinations, without causes of aberrant transaminase values or secondary causes of liver fat accumulation, determined by checking the medical history or performing laboratory tests[6, 7]. Transient elastography (TE) can be performed to accurately diagnose liver steatosis and advanced hepatopathy among adults as a non-invasive imaging method[8]. In the National Health and Nutrition Examination Survey (NHANES) during the recent cycle, liver ultrasound TE was included as a method for detecting liver steatosis and hepatic fibrosis based on the liver stiffness measurement (LSM) and controlled attenuation parameter (CAP). In this study, using the NHANES database, we analyzed the relationship between HTN and liver steatosis and fibrosis, which were measured based on CAP and LSM in adult participants.

Methods

Participants

In this cross-sectional study, data were obtained from the NHANES database (2017-March 2020 Pre-pandemic cycle). In the NHANES, health data on the US population were collected objectively. The data collection methodology is available on the NHANES website (http://www.cdc.gov/nchs/nhanes.htm)[9]. Of the 9,232 adults (≥ 20 years old) for whom information was available in the above-mentioned database, unqualified adults were eliminated as follows, one individual for whom blood pressure values were unavailable; 1,310 for whom LSM or CAP information was unavailable; 3,025 individuals positive for hepatitis C antibody, hepatitis B surface antigen, or with a history of alcoholism (≥ 3 and ≥ 4 drinks/day for women and men, respectively)[10]; 59 individuals for whom information on body mass index (BMI) was unavailable. Overall, data on 4,837 participants were included in the analysis. A flow chart describing the outline of our study is presented in Fig. 1.

Our survey protocols were approved by the National Center for Health Statistics Research Ethics Review Board. Written informed consent was obtained from all participants for data collection and the use of information. Our study maintained transparency following the guidelines of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[11, 12].

Variables in the study

Hypertension status was investigated in this study and was defined based on the following criteria: first, the questionnaire item that stated “ever told you had high blood pressure” represented the self-reported status of HTN; second, mean diastolic pressure > 90 mmHg and mean systolic pressure > 140 mmHg

were determined four times; third, the participants with HTN were identified based on their response to the questionnaire item “taking prescribed medication for hypertension”[13]. A FibroScan® system (model 502, V2 Touch) was used for performing liver ultrasound TE, and CAP was measured at ≥ 274 dB/m for liver steatosis, which indicated steatosis on liver ultrasound[14]. The result of the LSM (median, ≥ 8 kPa) confirmed fibrosis[15], which was measured using the FibroScan® model 502 V2 Touch in liver ultrasound TE that possessed an extra-large or moderate probe. Besides recording data on clinical and demographic factors, we extracted the data on several variables to be used as covariates, including age, gender, ethnicity, education level, BMI, family income-to-poverty ratio, smoked ≥ 100 cigarettes during the lifetime, and the levels of blood urea nitrogen (BUN), serum glucose, total cholesterol (TC), triglyceride (TG), serum uric acid (SUC), LDL cholesterol, aspartic acid transferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), and glycohemoglobin.

Statistical analysis

EmpowerStats (X&Y Solutions; Boston, MA) and R (version 3.4.3) were used for conducting statistical analyses, and $P < 0.05$ represented statistical significance. To determine the association between liver steatosis and fibrosis and HTN status, we constructed a multivariate logistic regression model. Three statistical models were considered for data analysis, including model 1 with unadjusted covariates, model 2 with adjusted age, gender, and ethnicity, and model 3 with adjusted covariates shown in Table 1. We also conducted subgroup analyses based on age, gender, ethnicity, and BMI.

Table 1
The characteristics of the participants

	Non-hypertension	hypertension	P-value
Age (years)	46.0 ± 16.3	60.8 ± 13.6	< 0.001
Sex (%)			0.908
Men	48.5	48.6	
Women	51.5	51.4	
Race			< 0.001
Non-Hispanic White	62.4	66.6	
Non-Hispanic Black	10.5	13.2	
Mexican American	9.7	5.3	
Other race	17.4	14.9	
Education level			< 0.001
Less than high school	10.7	12.4	
High school	25.2	32.1	
More than high school	64.1	55.4	
Body mass index (kg/m2)	28.8 ± 6.9	31.7 ± 7.5	< 0.001
Ratio of family income to poverty	3.3 ± 1.6	3.1 ± 1.6	0.002
Smoked at least 100 cigarettes in life (%)			< 0.001
Yes	35.8	45.6	
No	64.2	54.4	
Glycohemoglobin (%)	5.6 ± 0.8	6.1 ± 1.2	< 0.001
Serum glucose (mmol/L)	5.8 ± 1.4	6.8 ± 2.5	< 0.001
Alkaline phosphatase (U/L)	74.2 ± 23.7	79.9 ± 24.4	< 0.001
Alanine amino transferase (IU/L)	21.9 ± 15.0	22.4 ± 15.2	0.227
Aspartic acid transferase (IU/L)	21.2 ± 11.2	21.6 ± 12.2	0.269
Gamma-glutamyl transpeptidase (IU/L)	27.6 ± 48.9	31.0 ± 37.4	0.011

Continuous variables were presented as the mean ± SD, and P-values were determined by performing the Kruskal-Wallis H test (skewed distribution) and one-way ANOVA (normal distribution). Categorical variables were presented as a percentage, and the P-values were determined by performing a Chi-squared test

	Non-hypertension	hypertension	P-value
Serum uric acid (umol/L)	305.8 ± 77.3	333.5 ± 88.8	< 0.001
Blood urea nitrogen (mmol/L)	5.1 ± 1.5	6.1 ± 2.4	< 0.001
Total cholesterol ((mmol/L)	4.9 ± 1.1	4.8 ± 1.1	0.012
Triglyceride	1.2 ± 1.3	1.4 ± 1.0	< 0.001
LDL Cholesterol	3.0 ± 1.0	2.8 ± 0.9	< 0.001
Median controlled attenuation parameter (dB/m)	256.0 ± 59.3	286.1 ± 62.4	< 0.001
Liver steatosis (%)			< 0.001
Yes	37.0	58.4	
No	63.0	41.6	
Median liver stiffness (kpa)	5.5 ± 4.5	6.6 ± 5.2	< 0.001
Significant fibrosis (%)			< 0.001
Yes	8.2	16.5	
No	91.8	83.5	

Continuous variables were presented as the mean ± SD, and P-values were determined by performing the Kruskal-Wallis H test (skewed distribution) and one-way ANOVA (normal distribution). Categorical variables were presented as a percentage, and the P-values were determined by performing a Chi-squared test

Results

As shown in Table 1, the participants were characterized by their HTN status. Of the 4,837 participants enrolled, 2,375 were placed in the HTN group, while the remaining 2,462 participants were placed in the non-HTN group. The HTN patients were older, had higher BMI, higher ALP, GGT, glycohemoglobin, serum glucose, BUN, and uric acid levels, higher LSM and CAP values, and elevated liver steatosis and fibrosis rates than the non-HTN patients, but they had lower TC and LDL cholesterol levels than non-HTN patients.

Relationship between HTN status and CAP

After adjusting all confounders, our results showed that HTN status had a positive relationship with CAP (β = 9.7, 95% CI: 4.9–14.5; Table 2). The results of the subgroup analysis showed a stronger positive relationship among female participants (β = 10.1, 95% CI: 3.0–17.2) than among male participants (β = 8.9, 95% CI, 2.3–15.6) and also among participants who were 40–59 years old (β = 14.2, 95% CI: 6.8–21.6), non-Hispanic black (β = 16.8, 95% CI: 4.8–28.8), Non-Hispanic White (β = 10.2, 95% CI: 2.7–17.7),

and those who had BMI < 25 kg/m^2 (β = 13.2, 95% CI: 2.6–23.7) and BMI ≥ 25 kg/m^2 (β = 14.5, 95% CI: 6.7–22.2).

Table 2
Relationship between hypertension 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-hypertension	Reference	Reference	Reference
hypertension	30.1 (26.7, 33.6) < 0.001	28.4 (24.6, 32.2) < 0.001	9.7 (4.9, 14.5) <0.001
Stratified by sex			
Men (n = 2392)			
Non-hypertension	Reference	Reference	Reference
hypertension	31.3 (26.4, 36.2) < 0.001	31.5 (26.2, 36.8) < 0.001	8.9 (2.3, 15.6) 0.009
Women (n = 2445)			
Non-hypertension	Reference	Reference	Reference
hypertension	28.9 (24.1, 33.7) < 0.001	24.8 (19.4, 30.2) < 0.001	10.1 (3.0, 17.2) 0.005
Stratified by age			
20–39 age group (n = 1049)			
Non-hypertension	Reference	Reference	Reference
hypertension	35.0 (24.8, 45.2) < 0.001	35.0 (25.0, 45.0) < 0.001	6.7 (-5.1, 18.5) 0.268
40–59 age group (n = 1671)			
Non-hypertension	Reference	Reference	Reference
hypertension	32.9 (27.1, 38.8) < 0.001	33.5 (27.7, 39.4) < 0.001	14.2 (6.8, 21.6) < 0.001
60–80 age group (n = 2117)			
Non-hypertension	Reference	Reference	Reference
hypertension	21.4 (15.9, 26.9) < 0.001	22.6 (17.2, 28.1) < 0.001	6.2 (-1.4, 13.9) 0.111

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 β (95% CI, P)	Model 2 β (95% CI, P)	Model 3 β (95% CI, P)
Stratified by race			
Non-Hispanic White (n = 1742)			
Non-hypertension	Reference	Reference	Reference
hypertension	32.9 (27.3, 38.6) < 0.001	30.7 (24.6, 36.9) < 0.001	10.2 (2.7, 17.7) 0.008
Non-Hispanic Black (n = 1312)			
Non-hypertension	Reference	Reference	Reference
hypertension	25.8 (19.3, 32.4) < 0.001	19.9 (12.1, 27.7) < 0.001	16.8 (4.8, 28.8) 0.006
Mexican American (n = 544)			
Non-hypertension	Reference	Reference	Reference
hypertension	18.1 (7.3, 28.9) 0.001	11.3 (-0.6, 23.2) 0.063	-4.5 (-19.4, 10.4) 0.555
Other race (n = 1239)			
Non-hypertension	Reference	Reference	Reference
hypertension	34.2 (27.2, 41.1) < 0.001	30.3 (22.3, 38.2) < 0.001	9.8 (-0.6, 20.2) 0.066
Stratified by body mass index (BMI)			
BMI < 25 (kg/m^2) (n = 1125)			
Non-hypertension	Reference	Reference	Reference
hypertension	21.8 (16.3, 27.3) < 0.001	14.1 (8.1, 20.2) < 0.001	13.2 (2.6, 23.7) 0.015
BMI ≥ 25, < 30 (kg/m^2) (n = 1609)			
Non-hypertension	Reference	Reference	Reference

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 β (95% CI, P)	Model 2 β (95% CI, P)	Model 3 β (95% CI, P)
hypertension	11.1 (6.1, 16.1) < 0.001	5.5 (0.1, 11.0) 0.045	7.4 (-1.1, 15.8) 0.090
BMI ≥ 30 (kg/m^2) (n = 2103)			
Non-hypertension	Reference	Reference	Reference
hypertension	19.3 (14.5, 24.0) < 0.001	21.5 (16.3, 26.7) < 0.001	14.5 (6.7, 22.2) < 0.001
Model 1: No covariate adjustment			
Model 2: Adjustment for age, gender, and ethnicity			
Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin			

Relationship between HTN status and the incidence of liver steatosis

As determined by the model adjusted for all covariates (Table 3), HTN status showed a positive relationship with the liver steatosis rate (OR = 1.4, 95% CI: 1.1–1.8). In the subgroup analysis, a stronger relationship was found among men (OR = 1.6, 95% CI: 1.1–2.3) than among women (OR = 1.1, 95% CI: 0.7–1.5) and also among participants with BMI ≥ 25 < 30 kg/m^2 (OR = 1.7, 95% CI: 1.1–2.5), and among those who were non-Hispanic Black (OR = 1.9, 95% CI: 1.1–3.5).

Table 3
Relationship between hypertension status and the incidence of liver steatosis

	Model 1 OR (95% CI, P)	Model 2 OR (95% CI, P)	Model 3 OR (95% CI, P)
Non-hypertension	Reference	Reference	Reference
hypertension	1.8 (1.6, 2.1) < 0.001	1.8 (1.6, 2.1) < 0.001	1.4 (1.1, 1.8) 0.010
Stratified by sex			
Men (n = 2392)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.8 (1.5, 2.1) < 0.001	1.9 (1.6, 2.3) < 0.001	1.6 (1.1, 2.3) 0.007
Women (n = 2445)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.9 (1.6, 2.2) < 0.001	1.7 (1.4, 2.1) < 0.001	1.1 (0.7, 1.5) 0.745
Stratified by age			
20–39 age group (n = 1049)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.2 (1.6, 3.1) < 0.001	2.3 (1.6, 3.2) < 0.001	1.4 (0.7, 2.9) 0.386
40–59 age group (n = 1671)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.9 (1.6, 2.3) < 0.001	2.1 (1.7, 2.5) < 0.001	1.5 (1.0, 2.2) 0.071
60–80 age group (n = 2117)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.3 (1.1, 1.6) 0.002	1.4 (1.2, 1.7) < 0.001	1.3 (0.9, 1.8) 0.218

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 OR (95% CI, P)	Model 2 OR (95% CI, P)	Model 3 OR (95% CI, P)
Stratified by race			
Non-Hispanic White (n = 1742)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.0 (1.6, 2.4) < 0.001	2.0 (1.6, 2.4) < 0.001	1.4 (0.9, 2.1) 0.147
Non-Hispanic Black (n = 1312)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.0 (1.6, 2.5) < 0.001	1.8 (1.4, 2.4) < 0.001	1.9 (1.1, 3.5) 0.025
Mexican American (n = 544)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.5 (1.1, 2.2) 0.017	1.3 (0.9, 2.0) 0.174	0.9 (0.4, 2.1) 0.862
Other race (n = 1239)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.1 (1.6, 2.6) < 0.001	1.8 (1.4, 2.3) < 0.001	1.5 (0.9, 2.5) 0.095
Stratified by body mass index (BMI)			
BMI < 25 (kg/m^2) (n = 1125)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.4 (1.7, 3.4) < 0.001	1.8 (1.17, 2.7) 0.007	1.8 (0.9, 3.7) 0.096
BMI ≥ 25, < 30 (kg/m^2) (n = 1609)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.4 (1.1, 1.7) 0.001	1.2 (1.0, 1.5) 0.091	1.7 (1.1, 2.5) 0.010

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 OR (95% CI, P)	Model 2 OR (95% CI, P)	Model 3 OR (95% CI, P)
BMI ≥ 30 (kg/m^2) (n = 2103)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.4 (1.1, 1.7) < 0.001	1.5 (1.2, 1.8) < 0.001	1.3 (0.9, 1.8) 0.227
Model 1: No covariate adjustment			
Model 2: Adjustment for age, gender, and ethnicity			
Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin			

Relationship between the HTN status and LSM

After adjusting the model for all covariates, HTN status was positively associated with LSM (β = 0.6, 95% CI: 0.2–1.1; Table 4). In the subgroup analysis, a positive relationship was found among women (β = 0.6, 95% CI: 0.2–1.0) and also among participants who were 40–59 years old (β = 0.7, 95% CI: 0.2–1.3) and those with BMI ≥ 30 kg/m^2 (β = 1.6, 95% CI: 0.7–2.5).

Table 4
Relationship between hypertension status and the incidence of liver stiffness (kPa)

	Model 1 β (95% CI, P)	Model 2 β (95% CI, P)	Model 3 β (95% CI, P)
Non-hypertension	Reference	Reference	Reference
hypertension	1.1 (0.8, 1.3) < 0.001	1.1 (0.8, 1.4) < 0.001	0.6 (0.2, 1.1) 0.009
Stratified by sex			
Men (n = 2392)			
Non-hypertension	Reference	Reference	Reference
hypertension	0.8 (0.3, 1.2) < 0.001	0.9 (0.4, 1.4) < 0.001	0.6 (-0.2, 1.5) 0.153
Women (n = 2445)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.3 (1.0, 1.6) < 0.001	1.3 (1.0, 1.6) < 0.001	0.6 (0.2, 1.0) 0.004
Stratified by age			
20–39 age group (n = 1049)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.2 (0.4, 2.1) 0.004	1.1 (0.2, 1.9) 0.011	0.1 (-1.5, 1.8) 0.865
40–59 age group (n = 1671)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.6 (1.1, 2.0) < 0.001	1.5 (1.1, 2.0) < 0.001	0.7 (0.2, 1.3) 0.007
60–80 age group (n = 2117)			
Non-hypertension	Reference	Reference	Reference
hypertension	0.6 (0.1, 1.0) 0.009	0.6 (0.1, 1.0) 0.011	0.4 (-0.4, 1.1) 0.358
Stratified by race			

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 β (95% CI, P)	Model 2 β (95% CI, P)	Model 3 β (95% CI, P)
Non-Hispanic White (n = 1742)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.0 (0.5, 1.5) < 0.001	1.1 (0.6, 1.6) < 0.001	0.8 (-0.0, 1.7) 0.059
Non-Hispanic Black (n = 1312)			
Non-hypertension	Reference	Reference	Reference
hypertension	0.9 (0.4, 1.4) < 0.001	0.6 (0.0, 1.2) 0.037	0.7 (-0.3, 1.7) 0.184
Mexican American (n = 544)			
Non-hypertension	Reference	Reference	Reference
hypertension	0.9 (0.3, 1.5) 0.003	0.3 (-0.4, 0.9) 0.436	-0.4 (-1.3, 0.5) 0.371
Other race (n = 1239)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.5 (1.0, 2.0) < 0.001	1.5 (1.0, 2.1) < 0.001	0.5 (-0.2, 1.2) 0.129
Stratified by body mass index (BMI)			
BMI < 25 (kg/m^2) (n = 1125)			
Non-hypertension	Reference	Reference	Reference
hypertension	0.4 (0.1, 0.7) 0.009	0.3 (-0.0, 0.6) 0.077	0.0 (-0.6, 0.7) 0.910
BMI ≥ 25, < 30 (kg/m^2) (n = 1609)			
Non-hypertension	Reference	Reference	Reference
hypertension	0.6 (0.2, 1.0) 0.001	0.2 (-0.2, 0.6) 0.245	0.1 (-0.6, 0.8) 0.708
BMI ≥ 30 (kg/m^2) (n = 2103)			

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 β (95% CI, P)	Model 2 β (95% CI, P)	Model 3 β (95% CI, P)
Non-hypertension	Reference	Reference	Reference
hypertension	0.9 (0.4, 1.4) < 0.001	1.2 (0.6, 1.8) < 0.001	1.6 (0.7, 2.5) < 0.001
Model 1: No covariate adjustment			
Model 2: Adjustment for age, gender, and ethnicity			
Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin			

Relationship between HTN status and liver fibrosis

After adjusting the model for all covariates, HTN status showed a positive relationship with liver fibrosis (OR = 2.0, 95% CI: 1.3–3.0) (Table 5). In subgroup analysis, a positive relationship was recorded among women (OR = 2.6, 95% CI: 1.3–5.1) and also among participants who were 40–59 years old (OR = 2.3, 95% CI: 1.1–4.6), 60–80 years old (OR = 2.2, 95% CI: 1.2–4.1), non-Hispanic White (OR = 3.0, 95% CI: 1.6–5.9), and those who had BMI ≥ 30 kg/m^2 (OR = 2.0, 95% CI: 1.2–3.3) and BMI ≥ 25 < 30 kg/m^2 (OR = 3.0, 95% CI: 1.1–8.1).

Table 5
Relationship between hypertension status and the incidence of fibrosis

	Model 1 OR (95% CI, P)	Model 2 OR (95% CI, P)	Model 3 OR (95% CI, P)
Non-hypertension	Reference	Reference	Reference
hypertension	2.2 (1.9, 2.7) < 0.001	2.1 (1.7, 2.6) < 0.001	2.0 (1.3, 3.0) < 0.001
Stratified by sex			
Men (n = 2392)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.2 (1.7, 2.8) < 0.001	2.1 (1.6, 2.7) < 0.001	1.7 (1.0, 2.9) 0.050
Women (n = 2445)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.3 (1.8, 3.1) < 0.001	2.1 (1.5, 2.9) < 0.001	2.6 (1.3, 5.1) 0.006
Stratified by age			
20–39 age group (n = 1049)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.3 (1.4, 3.9) 0.002	2.2 (1.3, 3.7) 0.005	1.5 (0.5, 4.2) 0.481
40–59 age group (n = 1671)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.3 (1.7, 3.1) < 0.001	2.4 (1.8, 3.2) < 0.001	2.3 (1.1, 4.6) 0.024
60–80 age group (n = 2117)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.7 (1.3, 2.3) < 0.001	1.8 (1.3, 2.4) < 0.001	2.2 (1.2, 4.1) 0.015
Stratified by race			

Model 1: No covariate adjustment

Model 2: Adjustment for age, gender, and ethnicity

Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 OR (95% CI, P)	Model 2 OR (95% CI, P)	Model 3 OR (95% CI, P)
Non-Hispanic White (n = 1742)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.3 (1.7, 3.1) < 0.001	2.5 (1.8, 3.5) < 0.001	3.0 (1.6, 5.9) < 0.001
Non-Hispanic Black (n = 1312)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.1 (1.5, 3.1) < 0.001	1.8 (1.2, 2.7) 0.004	2.1 (0.7, 5.9) 0.166
Mexican American (n = 544)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.5 (0.9, 2.6) 0.098	0.9 (0.5, 1.6) 0.792	0.8 (0.2, 3.0) 0.792
Other race (n = 1239)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.7 (1.8, 3.9) < 0.001	2.6 (1.7, 4.1) < 0.001	1.9 (0.8, 4.8) 0.156
Stratified by body mass index (BMI)			
BMI < 25 (kg/m^2) (n = 1125)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.9 (1.7, 5.0) < 0.001	2.1 (1.1, 4.0) 0.018	3.0 (0.8, 10.7) 0.092
BMI ≥ 25, < 30 (kg/m^2) (n = 1609)			
Non-hypertension	Reference	Reference	Reference
hypertension	2.2 (1.5, 3.4) < 0.001	1.5 (1.0, 2.4) 0.063	3.0 (1.1, 8.1) 0.026

Model 1: No covariate adjustment
Model 2: Adjustment for age, gender, and ethnicity
Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin

	Model 1 OR (95% CI, P)	Model 2 OR (95% CI, P)	Model 3 OR (95% CI, P)
BMI ≥ 30 (kg/m^2) (n = 2103)			
Non-hypertension	Reference	Reference	Reference
hypertension	1.7 (1.3, 2.1) < 0.001	1.6 (1.3, 2.1) < 0.001	2.0 (1.2, 3.3) 0.004
Model 1: No covariate adjustment			
Model 2: Adjustment for age, gender, and ethnicity			
Model 3: Adjustment for all covariates including age, gender, ethnicity, education, BMI, family income-to-poverty ratio, smoked > 100 cigarettes during the lifetime, BUN, serum glucose, TC, TG, LDL cholesterol, SUC, ALP, ALT, AST, GGT, and glycohemoglobin			

Discussion

In this study, we determined the relationship between HTN status and the rates of liver steatosis and fibrosis in adults. Our results showed that HTN was associated with an increase in liver steatosis risk, which was more prominent in men, among non-Hispanic Black participants and those of other ethnicities, and those with BMI ≥ 25 < 30 kg/m^2. HTN status also showed a positive relationship with the incidence of fibrosis, and it was more prominent among women and also among participants who were older and those with BMI ≥ 25 kg/m^2.

Several epidemiological studies have found a bidirectional and mutual relationship between HTN and NAFLD, i.e., the risk of developing NAFLD increases when individuals have HTN, and the risk of developing HTN increases when individuals have NAFLD[16, 17]. Ciardullo et al. conducted a meta-analysis with 11 longitudinal studies and showed that NAFLD cases were associated with a 66% higher risk of developing HTN (HR: 1.66, CI: 1.38–2.01), though its prevalence varied with the age and BMI of the patients[18]. NAFLD cases with HTN are associated with an increased NAFLD progression risk compared to NAFLD cases without hypertension[19]. In another study (NHANES III), HTN was related to cardiovascular and all-cause mortality in NAFLD cases[5].

Non-alcoholic fatty liver disease (NAFLD) is closely associated with metabolic comorbidities like obesity[20], type 2 diabetes mellitus (T2DM)[21], or dyslipidemia[22], and therefore, it might be a hepatic manifestation of metabolic disorder. Besides causing hepatic morbidity and mortality, NAFLD can also induce clinical or subclinical CVDs. NAFLD patients have a high risk of HTN, cardiac arrhythmias, cardiomyopathy, and coronary heart disease (CHD), and it can also induce higher cardiovascular morbidity and mortality in the clinic. However, progressive NAFLD patients, like those with non-alcoholic steatohepatitis (NASH) and advanced fibrosis, are at the highest risk of developing CVDs[23].

Liver biopsy has the highest accuracy in diagnosing and staging the severity of NASH. However, it is expensive and invasive and might cause complications and interobserver variability among different pathological characteristics. Several non-invasive methods have been proposed for diagnosing NASH and staging liver fibrosis, including TE, which can be used for estimating liver stiffness as a surrogate for liver fibrosis[24, 25]. According to an NHANES study, HTN is independently related to NAFLD fibrosis; however, race-dependent differences also occur[26]. Our results also showed that HTN status was significantly related to CAP or LSM among individuals of a certain ethnicity, and it was not strongly related to CAP or LSM in the Mexican-American population.

Non-alcoholic fatty liver disease (NALFD) might develop into cirrhosis, which might include complications such as malignant tumors and is associated with CVDs or metabolic diseases[27, 28]. Genetic factors with susceptibility to NAFLD have an important effect on inflammation and lipid metabolism, thus affecting hypertension status[28–30]. Metabolic dysfunction is strongly related to the complicated mechanism involving the development of NAFLD; therefore, NAFLD might be called metabolic dysfunction-associated fatty liver disease (MAFLD). In this condition, metabolic dysfunction includes obesity, T2DM, hypertension, metabolic syndrome, and dyslipidemia[31–33]. NAFLD is an underestimated metabolic disorder and is closely related to a high incidence of prehypertension and hypertension rates[34]. HTN and NAFLD share common risk factors and show synergistic effects on the development and complications of the respective disorders. Hence, routine screening needs to be performed for HTN in NAFLD cases and people with lifestyle changes, such as physical activities and diet modifications, to prevent and manage HTN and NAFLD[35].

Our study had some limitations. First, this was a cross-sectional study, and thus, causal relationships were not determined. Second, the blood pressures of the participants were measured at one-time point, which might not precisely reflect the variation in blood pressure. Thus, hypertension was defined based on various criteria. Third, the CAP value that was used to define liver steatosis was not consistent with the LSM value that was used to define obvious in various studies based on the NAHENS 2017–2018 database[15, 36, 37]. Therefore, the sensitivity and specificity of the TE test were different for different cut-off values. Fourth, different measurements were obtained due to the different probes used with FibroScan[38, 39]. However, following specific protocols, elastography was performed by qualified and trained technicians[40]. Finally, the self-reported confounders might have induced individual bias, which can be reduced by using the NHANES data extracted by trained personnel using relevant procedures.

Conclusion

Overall, HTN showed a positive relationship with liver steatosis and fibrosis rates, which was stronger among subjects with BMI $\geq$ 25 kg/m^2 and was affected by the ethnicity of the participants. Our findings indicated that HTN screening in NAFLD patients could help in the prevention and management of HTN and NAFLD.

List Of Abbreviations

NAFLD
Non-alcoholic fatty liver disease
HTN
Hypertension
TE
Transient elastography
NHANES
National Health and Nutrition Examination Survey
CAP
Controlled attenuation parameter
LSM
Liver stiffness measurement
HbA1c
Glycohemoglobin
BMI
Body mass index
BUN
Blood urea nitrogen
GGT
Gamma-glutamyl transpeptidase
ALT
Alanine amino transferase
ALP
Alkaline phosphatase.

Declarations

Ethics approval and consent to participate

The NHANES protocols gained approval from Ethics Committee of National Center for Health Statistics. Each participant provided informed consent before participation.

Consent for publication

Not applicable.

Availability of data and materials

All data utilized or analyzed in this work can be obtained from NHANES website (http://www.cdc.gov/nchs/nhanes.htm).

Competing interests

All authors have claimed that there exist no competing interests.

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Authors' contributions

HJF, HY, YSZ, and JHC were responsible for collecting, analyzing data and writing manuscript. ZCL was in charge of designing this study and editing manuscript. All author(s) read and approved our eventual version.

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Figures

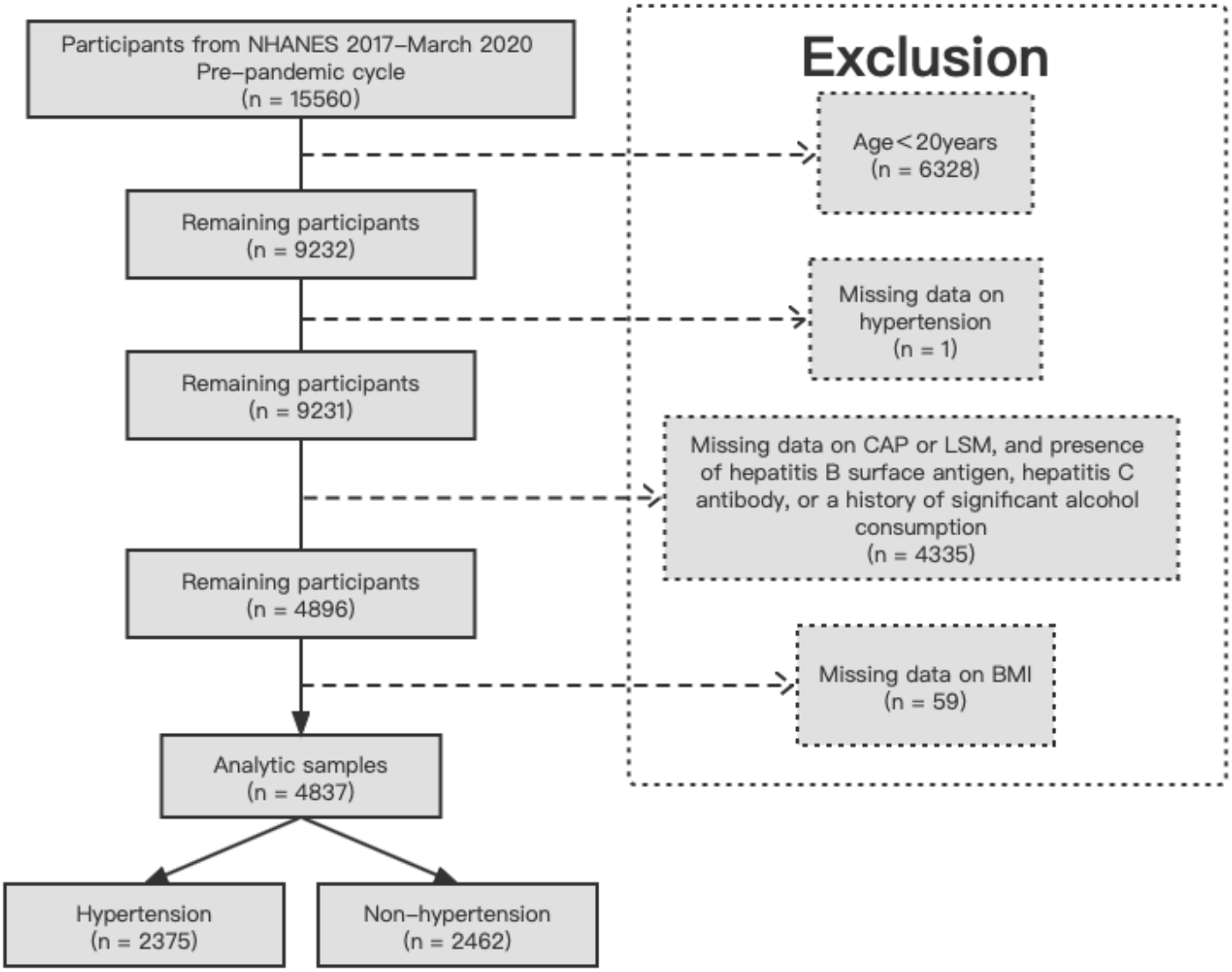

Figure 1

A flow chart describing the sample selection process.