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The association between the dietary index for gut microbiota and non-alcoholic fatty liver disease and liver fibrosis: evidence from NHANES 2017–2020

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Abstract

Background Imbalance in the gut microbiota is a key factor in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) and liver fibrosis. The Dietary Index for Gut Microbiota (DI-GM) integrates the potential relationship between diet and gut microbiota diversity. This study aims to investigate the association between DI-GM and the risk of NAFLD and liver fibrosis, providing theoretical support for dietary intervention strategies.

Methods This study utilized data from NHANES 2017–2020, including 6,181 eligible adult participants. The relationship between DI-GM and the risk of NAFLD and liver fibrosis was assessed using DI-GM quartiles, multivariate logistic regression, and restricted cubic spline (RCS) analysis. Subgroup analysis was performed to explore the predictive role of DI-GM in different populations. All analyses were weighted to ensure the representativeness of the results.

Results DI-GM was negatively associated with the risks of NAFLD and liver fibrosis. As DI-GM scores increased, the risk of NAFLD and liver fibrosis significantly decreased (52.81%, 43.16%, 40.40%, and 31.98%, $p < 0.05$; 17.52%, 9.04%, 7.21%, and 6.78%, $p < 0.05$). Multivariate logistic regression analysis revealed that, in the unadjusted model (Model 1), for each unit increase in DI-GM, the risk of NAFLD decreased by 6.9% (OR = 0.931, 95% CI: 0.886–0.979, $p < 0.001$), while the risk of liver fibrosis decreased by 15.6% (OR = 0.844, 95% CI: 0.757–0.941, $p < 0.05$). In the quartile analysis, individuals in the highest DI-GM quartile (Q4) had a 58% lower risk of NAFLD compared to those in the lowest quartile (Q1) (OR = 0.42, 95% CI: 0.219–0.806, $p < 0.001$). The results remained significant even after adjusting for covariates. RCS analysis showed that DI-GM had a nonlinear relationship with the risks of NAFLD and liver fibrosis, with inflection points at scores of 2 and 5, indicating enhanced protective effects.

Conclusion This study reveals a negative association between DI-GM and the risk of NAFLD and liver fibrosis, highlighting the potential role of healthy dietary patterns in the prevention and management of NAFLD and liver fibrosis through gut microbiota modulation, providing a theoretical basis for dietary interventions.

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Keywords NAFLD, DI-GM, NHANES, Gut microbiota, Dietary index

Introduction

Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent liver diseases globally and is strongly linked to metabolic disorders like obesity, diabetes, and cardiovascular diseases [1]. With shifts in dietary patterns, the prevalence of NAFLD has been steadily increasing worldwide, reaching 30.2%, posing a significant public health challenge [2, 3]. The pathophysiology of NAFLD is intricate, involving various factors including insulin resistance, fat accumulation, oxidative stress, and chronic inflammation [4]. If not intervened in a timely manner, NAFLD may further progress to liver fibrosis, eventually leading to cirrhosis or even liver cancer [5]. Therefore, early diagnosis and effective intervention of NAFLD are crucial to prevent the onset of liver fibrosis.

In recent years, an increasing number of studies have highlighted the role of the gut microbiota in NAFLD progression, proposing that dysbiosis may influence liver metabolism through several mechanisms, thereby contributing to the development of NAFLD [6, 7]. Diet, as a crucial factor influencing the gut microbiota, plays a significant role in the initiation and progression of NAFLD [8]. Different dietary patterns can influence the host's metabolic state by regulating the composition and function of the gut microbiota [9]. Traditional dietary assessment tools, such as the Healthy Eating Index (HEI) and the Mediterranean Diet Score (MDS), mainly evaluate dietary quality by aggregating dietary components, which may lack sensitivity to extreme manifestations of dietary patterns or the underlying traits of food behaviors [10]. Furthermore, these methods typically overlook the mediating role of the gut microbiota in the relationship between diet and health. Recently, Kase et al. [11] developed the Gut Microbiota Dietary Index (DI-GM), which particularly takes into account the relationship between diet, gut microbiota diversity, and health, offering a more refined quantitative tool for studying the dietary impact on the gut microbiota.

The DI-GM score was constructed based on a literature review of 14 food items or nutrients, incorporating foods that benefit gut health (e.g., fermented dairy products, chickpeas, soybeans) and foods detrimental to gut health (e.g., red meat, processed meats, refined grains) [11]. These components were selected based on existing research on their effects on gut microbiota diversity, short-chain fatty acid (SCFA) production, and the abundance of specific bacteria [11]. Growing evidence indicates that metabolites produced by the gut microbiota, including trimethylamine, secondary bile acids, short-chain fatty acids (SCFAs), and ethanol, play a significant role in the pathogenesis of NAFLD [7, 12, 13]. As a result, the DI-GM score may affect the production of these metabolites by modulating the gut microbiota, thereby influencing the onset of NAFLD. However, no study has yet explored the association between DI-GM and NAFLD risk, nor has its applicability been assessed in diverse populations.

Based on this, the aim of this study is to systematically assess the risk association between DI-GM and NAFLD as well as liver fibrosis using the large sample data from NHANES 2017–2020. We hypothesize that a higher DI-GM score, reflecting a healthier dietary pattern, is associated with a lower risk of NAFLD and liver fibrosis, which may be related to the impact of diet on the gut microbiota. Through this analysis, we hope to reveal the potential of DI-GM as a dietary quality indicator in predicting NAFLD and liver fibrosis, and provide new theoretical insights for future dietary intervention strategies.

Materials and methods

Data and sample sources

This study utilized data from NHANES conducted by the National Center for Health Statistics (NCHS). NHANES is a comprehensive survey designed to collect representative data on the health and nutritional status of U.S. civilians, encompassing demographics, socioeconomic status, dietary habits, and health-related issues. To ensure sample diversity, NHANES employs a stratified, multistage probability sampling method to select nationally representative participants. The study protocol was approved by the Ethics Review Board of the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC), and all participants signed written informed consent forms. The data are publicly available at https://www.cdc.gov/nchs/nhanes/.

This study primarily analyzes the health data of adults from the NHANES 2017–2020 cycle. The initial sample size consisted of 15,560 participants. We initially excluded individuals under 20 years old, followed by the exclusion of participants missing DI-GM and CAP (controlled attenuated parameter) data. Furthermore, individuals with heavy drinking (defined as more than 4 drinks per day), viral hepatitis, and autoimmune hepatitis diagnoses were excluded. The final analysis included 6,181 participants, among whom 2,718 were diagnosed with non-alcoholic fatty liver disease (NAFLD). The sample selection procedure is detailed in Fig. 1.

Exposure factors

Two dietary recall interviews were conducted in the NHANES study. The first assessment was conducted at the MEC through a 24-hour dietary recall interview, and

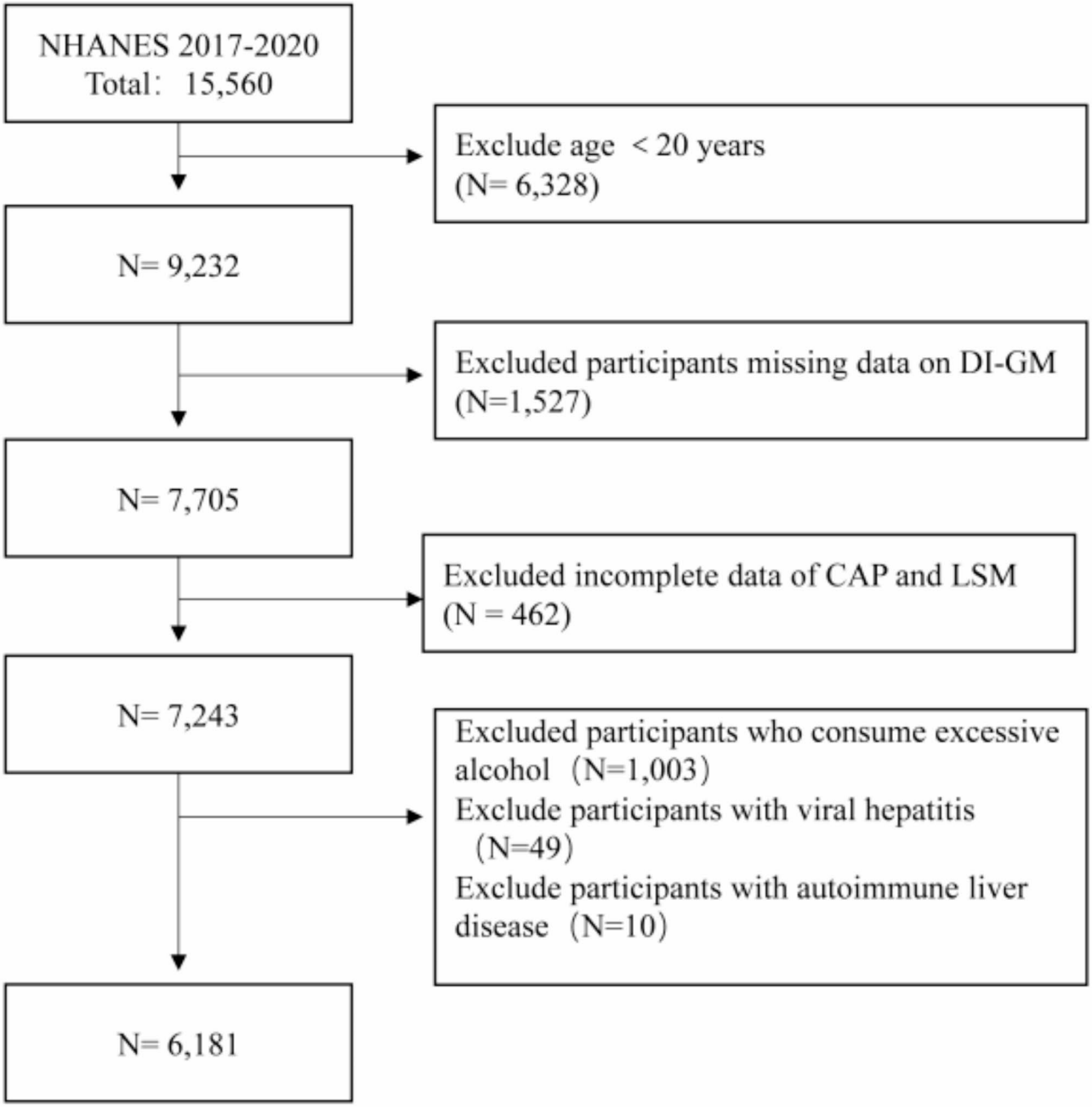

Fig. 1 Flow chart of the participants selection process

the second assessment was carried out via a telephone interview, which recorded detailed and comprehensive information on participants' dietary intake over the past 24 h, including all foods and beverages. Based on the study by Kase et al., 14 foods and nutrients were included in the DI-GM score, consisting of 10 foods beneficial to gut health and 4 foods detrimental to gut health [11]. For beneficial foods, participants whose intake exceeded the gender-specific median were given a score of 1, and those below the median received a score of 0. Conversely, for detrimental foods, participants whose intake exceeded the gender-specific median were assigned a score of 0, while those below the median were assigned a score of 1. The DI-GM score is derived by summing the scores of each component, ranging from 0 to 14. A higher DI-GM score reflects a healthier gut microbiota.

Outcome variables

Clinicians commonly use vibration-controlled transient elastography (VCTE) and liver stiffness measurement (LSM) as non-invasive techniques to assess the prevalence and severity of NAFLD and liver fibrosis. These

methods have been shown to be highly reliable. In the NHANES study, during the 2017–2018 period, researchers used devices equipped with the FibroScan® model 502 V2 Touch to conduct VCTE assessments on participants. NAFLD was diagnosed when the controlled attenuation parameter (CAP) value was ≥ 274 dB/m, while liver fibrosis was diagnosed when the LSM value was ≥ 8.2 kPa [14]. Based on whether participants met these diagnostic criteria, they were coded as 1 (meeting the criteria) or 0 (not meeting the criteria).

Covariates

This study, based on existing literature and clinical considerations, incorporated multiple confounding factors, including age, gender, race/ethnicity, education level, marital status, family income and poverty ratio (PIR), protein, carbohydrate, total sugars, dietary fiber, total fat, BMI, waist circumference (WC), blood pressure (BP), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), HbA1c, insulin (INS), smoking status, diabetes, hypertension, and physical activity (V/MPA). Race/ethnicity was categorized into: Mexican-American, non-Hispanic Asian, non-Hispanic Black, non-Hispanic White, other Hispanic, and other/multiracial. Education level was classified into three levels: high school or below, some college education, and college graduate or higher. Marital status was classified into: unmarried, married or cohabiting, and widowed or divorced. PIR was categorized into three groups: <1.30, 1.30–3.49, and ≥ 3.50. BMI was calculated by dividing weight (in kilograms) by the square of height (in meters). The diagnosis of hypertension was determined by a doctor's diagnosis or the use of antihypertensive medications. Smoking status was determined by whether the individual had smoked 100 cigarettes; those who answered "yes" were classified as smokers. V/MPA was defined as participating in at least 10 min of V/MPA in a typical week (2005–2020 cycle), leading to significant sweating, or a notable increase in breathing or heart rate. Diabetes diagnosis was defined by meeting one of the following criteria: (1) HbA1c ≥ 6.5%; (2) FPG ≥ 7.0 mmol/L; (3) a doctor's diagnosis of diabetes; or (4) taking antidiabetic medication or insulin. All covariates were extracted from the NHANES database and standardized prior to inclusion in the analysis model to control for confounding factors affecting the results.

Statistical methods

All data analyses in this study took into account the complex sampling design of NHANES and used weighted statistical methods to ensure the representativeness and robustness of the results. NHANES ensures national sample representativeness through multi-stage probability sampling. Following the recommendations of the National Center for Health Statistics (NCHS), sampling weights (WTMECPRP), pseudo-strata (SDMVSTRA), and pseudo-cluster (SDMVPSU) were applied during analysis to reflect the complexity of the design.

First, participants were grouped based on the presence or absence of non-alcoholic fatty liver disease (NAFLD), and further divided into quartiles based on DI-GM scores. For continuous variables that follow a normal distribution, weighted Student's t-test (for two-group comparison) or weighted one-way analysis of variance (ANOVA) (for multiple-group comparison) were used; for continuous variables that do not follow a normal distribution, weighted Mann-Whitney U-test (for two-group comparison) or weighted Kruskal-Wallis test (for multiple-group comparison) were used. Comparisons of categorical variables were performed using weighted chi-square tests. In all statistical descriptions, continuous variables are presented as weighted mean ± standard deviation, and categorical variables are presented as unweighted frequency and weighted percentage.

To further explore the association between DI-GM and NAFLD risk, subgroup analyses were performed based on key categorical variables, including gender, race, education level, PIR, marital status, smoking status, hypertension, diabetes, and physical activity. A multivariable logistic regression model was used to assess differences in the predictive effects of DI-GM across different subgroups.

To evaluate the relationship between DI-GM and NAFLD, three multivariable logistic regression models were constructed. Prior to modeling, variance inflation factor (VIF) analysis was conducted to assess multicollinearity among covariates. Model 1 was unadjusted for covariates, Model 2 adjusted for gender, age, and race, and Model 3 further adjusted for education level, marital status, PIR, V/MPA, hypertension, diabetes, smoking, protein, carbohydrate, total sugars, dietary fiber, total fat, BMI, WC, BP, TC, TG, HDL-C, LDL-C, HbA1c, and insulin (INS). In regression analysis, DI-GM was assessed both as a continuous variable and by quartile stratification. The results of each model were reported as odds ratios (ORs) with 95% confidence intervals (CIs). To explore the non-linear relationship between DI-GM and NAFLD risk, restricted cubic splines (RCS) analysis was performed, and the "smart filtering of cubic spline nodes" and "threshold effect" techniques were used to calculate the node positions and threshold points for each model.

Finally, to validate the robustness of the models, sensitivity analyses were performed, including adjustments for different combinations of covariates, removal of extreme values, and stepwise regression analysis, to assess changes in the non-linear relationships of the models. All statistical analyses used a two-tailed P-value < 0.05 as the

significance threshold. Data analysis was conducted using DecisionLinnc 1.0 software [15], and all results were verified multiple times to ensure the accuracy and robustness of the analysis.

Results

Baseline characteristics of the study population

This study included a total of 6,181 participants, with an average age of 47.72 years, comprising 2,718 NAFLD participants and 632 Liver Fibrosis participants. Among the overall sample, 45.76% (2,797 individuals) were male and 54.24% (3,384 individuals) were female. Compared to the Non-NAFLD group, the NAFLD group showed significantly higher intake levels of protein, dietary fiber, total fat, as well as higher SBP, DBP, WC, INS levels, FBG, HbA1c, TC, TG, and LDL-C ($p < 0.05$). In contrast, HDL-C and DI-GM scores were significantly lower in the NAFLD group ($p < 0.05$). Additionally, there were significant differences between the two groups in terms of gender, race, education level, marital status, BMI, diabetes, and hypertension ($p < 0.05$). Similarly, a similar trend was found in the comparison between Non-Liver Fibrosis and Liver Fibrosis. More detailed information is presented in Table 1.

Quantitative relationship between baseline characteristics and DI-GM quartiles

To explore the dose-response relationship between DI-GM and baseline characteristics of the participants, we divided the participants into four quartiles based on their DI-GM scores (Q1-Q4). The results showed that compared to the lower quartiles of DI-GM, participants in the higher DI-GM quartiles had significantly lower DBP, CAP, LSM, WC, and INS levels ($p < 0.05$), while HDL-C levels were significantly higher ($p < 0.001$). Furthermore, significant differences in the distribution of gender, race, education level, marital status, PIR, and BMI were observed ($p < 0.05$). Notably, as the quartiles of the DI-GM increased, the prevalence of NAFLD significantly decreased (52.81% vs. 43.16% vs. 40.40% vs. 31.98%, $p < 0.05$), as did the prevalence of liver fibrosis (17.52% vs. 9.04% vs. 7.21% vs. 6.78%, $p < 0.05$). Further details are provided in Table 2.

Association between DI-GM quartiles and NAFLD or liver fibrosis risk

To further explore the relationship between DI-GM and NAFLD or Liver fibrosis, we conducted multivariable logistic regression analysis. As shown in Table 3, in the unadjusted model (Model 1), DI-GM as a continuous variable was significantly associated with the risk of NAFLD or Liver fibrosis. Specifically, for each unit increase in DI-GM, the risk of NAFLD decreased by 6.9% (OR = 0.931, 95% CI: 0.886–0.979, $p < 0.05$), while the risk of liver fibrosis decreased by 15.6% (OR = 0.844, 95% CI: 0.757–0.941, $p < 0.05$).

Additionally, when DI-GM was analyzed by quartiles, individuals in the highest quartile (Q4) had a significantly lower risk of NAFLD compared to those in the lowest quartile (Q1), with an OR of 0.42 (95% CI: 0.219–0.806, $p < 0.001$), corresponding to a 58% reduction in NAFLD risk. Even after adjusting for confounders such as gender, age, and race in Model 2, and further adjusting for all potential covariates in Model 3, the results remained significant, indicating the robustness of the association between DI-GM and NAFLD or Liver fibrosis.

These findings suggest that DI-GM may have a protective effect against NAFLD or Liver fibrosis, and this association is not confounded by basic demographic variables.

Subgroup analysis

To further explore the predictive role of DI-GM on the risk of NAFLD in different populations, we conducted subgroup analyses, considering multiple factors such as gender, race, education level, and others (see Fig. 2). The analysis results indicate that the relationship between DI-GM and NAFLD risk followed a consistent trend across different subgroups, including gender, race, education level, marital status, PIR, BMI, smoking, V/MPA, hypertension, and diabetes. Furthermore, no significant interactions were found (p for interaction > 0.05), suggesting that the effect of DI-GM on NAFLD risk may not differ significantly across these subgroups.

Restricted cubic spline analysis

To investigate the nonlinear relationship between DI-GM and NAFLD or Liver fibrosis risk, we performed a restricted cubic spline (RCS) analysis. The results (see Fig. 3) indicated a significant nonlinear relationship between DI-GM and NAFLD or Liver fibrosis risk ($p < 0.05$). This nonlinear association was consistently observed in the unadjusted model (Model 1), the partially adjusted model (Model 2), and the fully adjusted model (Model 3), suggesting that the effect of DI-GM on NAFLD or Liver fibrosis risk is not monotonic.

Further threshold analysis revealed that the RCS analysis identified key knot points at 3, 5, and 7 across the three models, which represent critical cutoff points for the DI-GM variable. Specifically, when the DI-GM value exceeds 5, the odds ratio (OR) becomes less than 1, indicating a significant reduction in NAFLD or Liver fibrosis risk. This finding suggests that improvements in DI-GM may have a more pronounced protective effect after crossing a certain threshold.

Additionally, further analysis using the RCS model revealed that the inflection points for the effects of DI-GM on both NAFLD and liver fibrosis occurred at

Table 1 Baseline characteristics of participants

Characteristic	Overall *N* = 6,181	Non-NAFLD *N* = 3,463	NAFLD *N* = 2,718	*p*-value	Non-Liver Fibrosis *N* = 5,549	Liver Fibrosis *N* = 632	*p*-value
Age(years)	47.72 ± 17.27	45.62 ± 17.69	50.53 ± 16.28	< 0.001	47.25 ± 17.32	52.40 ± 16.11	< 0.001
Protein(g)	3.09 ± 5.71	3.04 ± 5.74	3.15 ± 5.66	0.030	4.42 ± 9.45	4.89 ± 10.03	0.903
Carbohydrate(g)	12.54 ± 17.10	11.81 ± 16.40	13.52 ± 17.95	0.063	15.78 ± 25.48	19.96 ± 32.45	0.495
Total sugars(g)	6.01 ± 11.05	5.62 ± 10.54	6.55 ± 11.68	0.159	7.76 ± 17.98	10.04 ± 23.90	0.773
Dietary fiber(g)	0.68 ± 1.22	0.65 ± 1.18	0.72 ± 1.27	0.037	0.90 ± 1.86	0.96 ± 2.08	0.727
Total fat(g)	3.91 ± 6.69	3.65 ± 6.52	4.27 ± 6.90	0.003	5.25 ± 10.14	6.07 ± 10.86	0.748
SBP(mmHg)	121.40 ± 17.14	119.42 ± 17.36	124.03 ± 16.47	< 0.001	120.86 ± 17.03	126.83 ± 17.31	< 0.001
DBP(mmHg)	73.93 ± 10.74	72.10 ± 10.44	76.36 ± 10.67	< 0.001	73.61 ± 10.56	77.09 ± 12.01	< 0.001
CAP(dB/m)	263.32 ± 63.03	218.63 ± 35.92	323.24 ± 36.06	< 0.001	257.79 ± 60.25	319.19 ± 63.32	< 0.001
LSM(kPa)	5.81 ± 4.75	4.96 ± 3.01	6.94 ± 6.20	< 0.001	4.90 ± 1.25	14.94 ± 11.98	< 0.001
WC(cm)	100.15 ± 17.08	92.15 ± 13.62	110.88 ± 15.28	< 0.001	98.36 ± 15.73	118.68 ± 19.38	< 0.001
TC(mmol/L)	4.84 ± 1.02	4.78 ± 1.00	4.92 ± 1.05	0.004	4.86 ± 1.02	4.72 ± 1.06	0.003
INS(μU/mL)	13.07 ± 17.81	9.15 ± 12.32	18.43 ± 22.23	< 0.001	12.03 ± 11.98	24.69 ± 46.03	< 0.001
HDL-C(mmol/L)	1.39 ± 0.40	1.50 ± 0.40	1.26 ± 0.36	< 0.001	1.41 ± 0.40	1.24 ± 0.38	< 0.001
HbA1c(%)	5.66 ± 0.93	5.45 ± 0.67	5.94 ± 1.13	< 0.001	5.60 ± 0.86	6.23 ± 1.34	< 0.001
TG(mmol/L)	1.23 ± 1.00	0.98 ± 0.61	1.58 ± 1.29	< 0.001	1.21 ± 0.98	1.45 ± 1.20	< 0.001
LDL-C(mmol/L)	2.83 ± 0.90	2.77 ± 0.87	2.92 ± 0.95	0.007	2.84 ± 0.90	2.74 ± 0.96	0.173
FBG(mmol/L)	6.06 ± 1.74	5.67 ± 1.14	6.59 ± 2.23	< 0.001	5.96 ± 1.60	7.12 ± 2.71	< 0.001
DI-GM	4.86 ± 1.70	4.94 ± 1.68	4.74 ± 1.73	0.007	4.90 ± 1.69	4.42 ± 1.82	0.001
Sex				< 0.001			< 0.001
Male	2,797 (45.76%)	1,432 (40.64%)	1,365 (52.63%)		2,454 (44.67%)	343 (56.78%)	
Female	3,384 (54.24%)	2,031 (59.36%)	1,353 (47.37%)		3,095 (55.33%)	289 (43.22%)	
Race				< 0.001			0.866
Mexican American	717 (7.96%)	299 (5.91%)	418 (10.71%)		637 (7.94%)	80 (8.19%)	
Other Hispanic	632 (7.32%)	344 (7.35%)	288 (7.28%)		573 (7.42%)	59 (6.29%)	
Non-Hispanic White	2,135 (63.85%)	1,159 (64.36%)	976 (63.17%)		1,899 (63.71%)	236 (65.29%)	
Non-Hispanic Black	1,651 (11.20%)	1,041 (12.71%)	610 (9.19%)		1,476 (11.23%)	175 (10.94%)	
Other Race	1,046 (9.66%)	620 (9.67%)	426 (9.66%)		964 (9.70%)	82 (9.29%)	
Education				0.002			0.001
Less than high school	1,027 (9.32%)	539 (8.75%)	488 (10.08%)		908 (9.05%)	119 (12.03%)	
High school or GED	1,433 (26.13%)	778 (24.09%)	655 (28.87%)		1,268 (25.23%)	165 (35.25%)	
College or above	3,721 (64.55%)	2,146 (67.16%)	1,575 (61.05%)		3,373 (65.72%)	348 (52.72%)	
Marital_status				< 0.001			0.148
Never married	1,236 (19.80%)	815 (23.79%)	421 (14.45%)		1,135 (20.22%)	101 (15.57%)	
Married or cohabit	3,602 (62.49%)	1,896 (58.01%)	1,706 (68.50%)		3,230 (62.37%)	372 (63.73%)	
Widowed or divorced	1,343 (17.71%)	752 (18.20%)	591 (17.05%)		1,184 (17.41%)	159 (20.70%)	
PIR				0.331			0.004
< 1.30	1,414 (15.21%)	803 (15.29%)	611 (15.11%)		1,276 (15.29%)	138 (14.45%)	
1.30–3.49	2,868 (40.68%)	1,588 (39.70%)	1,280 (41.99%)		2,534 (39.67%)	334 (50.90%)	
≥ 3.50	1,899 (44.11%)	1,072 (45.02%)	827 (42.90%)		1,739 (45.05%)	160 (34.65%)	
BMI				< 0.001			< 0.001
< 25	1,547 (26.72%)	1,352 (42.18%)	195 (6.00%)		1,488 (28.52%)	59 (8.56%)	
25–30	1,999 (32.01%)	1,229 (36.11%)	770 (26.51%)		1,889 (33.72%)	110 (14.69%)	
≥ 30	2,635 (41.27%)	882 (21.72%)	1,753 (67.50%)		2,172 (37.76%)	463 (76.74%)	
Diabetes				< 0.001			< 0.001
No	5,094 (87.31%)	3,125 (94.48%)	1,969 (77.70%)		4,716 (89.49%)	378 (65.26%)	
Yes	1,087 (12.69%)	338 (5.52%)	749 (22.30%)		833 (10.51%)	254 (34.74%)	
Smoke status				0.176			0.231
No	3,909 (61.95%)	2,245 (63.09%)	1,664 (60.42%)		3,545 (62.25%)	364 (58.94%)	
Yes	2,272 (38.05%)	1,218 (36.91%)	1,054 (39.58%)		2,004 (37.75%)	268 (41.06%)	
VMPA				0.676			0.936
No	3,227 (47.79%)	1,822 (48.11%)	1,405 (47.36%)		2,871 (47.81%)	356 (47.56%)	

Table 1 (continued)

Characteristic	Overall *N* = 6,181	Non-NAFLD *N* = 3,463	NAFLD *N* = 2,718	*p*-value	Non-Liver Fibrosis *N* = 5,549	Liver Fibrosis *N* = 632	*p*-value
Yes	2,954 (52.21%)	1,641 (51.89%)	1,313 (52.64%)		2,678 (52.19%)	276 (52.44%)	
Hypertension				< 0.001			< 0.001
No	3,915 (69.07%)	2,449 (77.91%)	1,466 (57.24%)		3,626 (70.74%)	289 (52.27%)	
Yes	2,266 (30.93%)	1,014 (22.09%)	1,252 (42.76%)		1,923 (29.26%)	343 (47.73%)	

Note Categorical variables are presented as unweighted frequencies and weighted percentages, and group comparisons are performed using weighted chi-square tests. Continuous variables are presented as weighted means ± standard deviations, and group comparisons are performed using weighted t-tests or weighted Mann-Whitney tests

different values: the inflection point for NAFLD was near a value of 2, while for liver fibrosis it was at 5. Below these thresholds, the relationship between DI-GM and the respective risks remained relatively flat, but above these inflection points, the protective effect of DI-GM on both NAFLD and liver fibrosis gradually intensified. These results suggest that after DI-GM reaches certain critical values, its impact on both NAFLD and liver fibrosis risk becomes more pronounced, potentially reflecting stronger underlying biological mechanisms. For clinical practice, a DI-GM score below 2 may indicate a higher risk for NAFLD and liver fibrosis, suggesting that early dietary interventions aimed at improving gut microbiome health may be warranted. In contrast, DI-GM scores above 2 could signal a marked reduction in risk, with scores above 5 potentially offering more robust protection. These inflection points provide valuable guidance for clinicians to tailor dietary recommendations and preventive strategies, highlighting the importance of dietary patterns that promote gut health.

Sensitivity and robustness analyses

To evaluate the robustness of the models, we conducted sensitivity analyses on both the restricted cubic spline (RCS) analysis and the logistic regression models. For the logistic regression models, we progressively removed key covariates such as BMI, protein, carbohydrate, total sugars, dietary fiber, total fat, hypertension, and diabetes, and excluded extreme values and outliers within the relevant variables. Even after these adjustments, the association between DI-GM and NAFLD risk remained significant ($p < 0.05$), validating the robustness of the model results.

In the RCS analysis, regardless of whether variables such as BMI, waist circumference (WC), protein, carbohydrate, total sugars, dietary fiber, total fat, hypertension, and diabetes were randomly removed or added, the non-linear relationship between DI-GM and NAFLD risk remained significant ($p < 0.05$). These results further support the stable association between DI-GM and NAFLD risk, indicating that this relationship holds under various conditions.

Discussion

This study analyzed the NHANES 2017–2020 data, including 6,181 participants, and systematically evaluated the relationship between the DI-GM and NAFLD or liver fibrosis. Our results indicate that the DI-GM score in the NAFLD or liver fibrosis group was significantly lower than that in the Non-NAFLD or Non-liver fibrosis group. As the DI-GM score increased, the risk of NAFLD or liver fibrosis gradually decreased. Specifically, with each unit increase in DI-GM, the risk of NAFLD or liver fibrosis decreased by 6.9% and 15.6%, and this relationship exhibited a significant nonlinear trend. These results suggest that a higher DI-GM score is associated with a reduced risk of NAFLD or Liver fibrosis, providing new theoretical evidence for dietary interventions and the early prevention of NAFLD or Liver fibrosis.

Although there is currently no specific study directly exploring the relationship between DI-GM and NAFLD or liver fibrosis, existing research has demonstrated that the gut microbiome plays a crucial role in the pathogenesis of both NAFLD and liver fibrosis. Dysbiosis, particularly alterations in the composition and function of the gut microbiota, is considered one of the key pathological factors underlying the development of NAFLD and liver fibrosis. Increasing evidence suggests that the gut microbiome directly influences the host's metabolic state through its metabolic products [16, 17]. For instance, short-chain fatty acids (SCFAs), which are products of gut microbiota fermenting dietary fibers, have been shown to be closely associated with insulin sensitivity and lipid metabolism [18, 19]. SCFAs not only reduce intestinal permeability by enhancing gut barrier function but also regulate hepatic fat synthesis and oxidation processes, thereby reducing fat deposition in the liver [20]. Moreover, trimethylamine (TMA) and its metabolite trimethylamine-N-oxide (TMAO) have also been implicated in the progression of NAFLD and liver fibrosis, with studies showing that TMAO exacerbates liver disease by modulating bile acid metabolism and inhibiting FXR signaling pathways [21]. Several meta-analyses have indicated that gut microbiota therapies, including probiotics, synbiotics, and prebiotics, can significantly lower blood lipids (such as TG, TC, and LDL-C), blood glucose levels, and BMI, thereby improving the progression of

Table 2 Baseline characteristics by DI-GM quartiles

Characteristic	Q1(0–2) *N* = 500	Q2(3–5) *N* = 3,719	Q3(6–8) *N* = 1,851	Q4(9–11) *N* = 111	*p*-value
Age(years)	44.33 ± 17.18	46.81 ± 17.46	50.07 ± 16.76	48.72 ± 15.99	< 0.001
Protein(g)	3.16 ± 6.12	3.00 ± 5.57	3.19 ± 5.90	3.41 ± 5.01	0.194
Carbohydrate(g)	13.18 ± 18.59	12.60 ± 17.20	12.30 ± 16.83	12.12 ± 13.17	0.949
Total sugars(g)	6.41 ± 12.28	6.11 ± 11.15	5.74 ± 10.71	6.20 ± 9.19	0.795
Dietary fiber(g)	0.55 ± 0.94	0.64 ± 1.17	0.77 ± 1.36	0.79 ± 1.30	0.302
Total fat(g)	4.65 ± 7.12	3.93 ± 6.75	3.74 ± 6.56	3.60 ± 5.45	0.699
SBP(mmHg)	121.69 ± 16.64	121.63 ± 17.27	121.22 ± 17.09	116.79 ± 15.03	0.175
DBP(mmHg)	75.02 ± 11.04	74.24 ± 10.86	73.37 ± 10.41	69.83 ± 10.19	0.019
CAP(dB/m)	276.88 ± 65.28	264.67 ± 62.95	259.75 ± 62.21	234.87 ± 57.07	0.005
LSM(kPa)	7.12 ± 7.25	5.71 ± 3.92	5.75 ± 5.48	4.91 ± 2.00	0.004
WC(cm)	105.96 ± 18.74	100.70 ± 17.16	98.42 ± 16.32	91.82 ± 13.28	< 0.001
TC(mmol/L)	4.84 ± 1.03	4.82 ± 1.02	4.89 ± 1.02	4.72 ± 1.15	0.134
INS(μU/mL)	15.56 ± 15.03	13.87 ± 21.07	11.39 ± 11.55	10.02 ± 7.00	< 0.001
HDL-C(mmol/L)	1.33 ± 0.39	1.36 ± 0.38	1.47 ± 0.43	1.51 ± 0.42	< 0.001
HbA1c(%)	5.71 ± 1.01	5.67 ± 0.95	5.64 ± 0.88	5.49 ± 0.55	0.271
TG(mmol/L)	1.38 ± 2.02	1.25 ± 0.96	1.18 ± 0.73	1.05 ± 0.75	0.299
LDL-C(mmol/L)	2.93 ± 0.94	2.83 ± 0.91	2.84 ± 0.89	2.61 ± 0.98	0.547
FBG(mmol/L)	6.02 ± 1.71	6.07 ± 1.67	6.06 ± 1.90	5.82 ± 1.14	0.736
DI-GM	1.70 ± 0.56	4.15 ± 0.78	6.57 ± 0.73	9.19 ± 0.47	< 0.001
Sex					0.006
Male	243 (48.82%)	1,731 (47.25%)	784 (43.55%)	39 (28.12%)	
Female	257 (51.18%)	1,988 (52.75%)	1,067 (56.45%)	72 (71.88%)	
Race					< 0.001
Mexican American	47 (9.66%)	444 (8.24%)	221 (7.40%)	5 (3.13%)	
Other Hispanic	52 (8.58%)	388 (7.65%)	180 (6.65%)	12 (3.95%)	
Non-Hispanic White	153 (58.51%)	1,254 (62.40%)	684 (66.99%)	44 (74.53%)	
Non-Hispanic Black	192 (16.94%)	1,091 (12.93%)	355 (7.30%)	13 (3.33%)	
Other Race	56 (6.30%)	542 (8.78%)	411 (11.66%)	37 (15.07%)	
Education					< 0.001
Less than high school	91 (10.59%)	688 (10.60%)	237 (6.88%)	11 (6.46%)	
High school or GED	143 (34.20%)	949 (29.21%)	331 (19.48%)	10 (14.35%)	
College or above	266 (55.21%)	2,082 (60.19%)	1,283 (73.64%)	90 (79.19%)	
Marital_status					0.002
Never married	151 (28.14%)	787 (21.21%)	280 (15.20%)	18 (21.97%)	
Married or cohabit	241 (55.27%)	2,137 (61.83%)	1,145 (64.78%)	79 (70.40%)	
Widowed or divorced	108 (16.60%)	795 (16.96%)	426 (20.01%)	14 (7.62%)	
PIR					< 0.001
< 1.30	132 (17.73%)	949 (17.39%)	320 (11.03%)	13 (9.46%)	
1.30–3.49	267 (48.98%)	1,756 (42.02%)	808 (36.95%)	37 (32.14%)	
≥ 3.50	101 (33.29%)	1,014 (40.59%)	723 (52.02%)	61 (58.40%)	
BMI					< 0.001
< 25	105 (18.92%)	875 (24.34%)	526 (31.86%)	41 (41.16%)	
25–30	135 (22.37%)	1,181 (32.85%)	632 (31.53%)	51 (47.87%)	
≥ 30	260 (58.71%)	1,663 (42.82%)	693 (36.61%)	19 (10.98%)	
NAFLD					0.005
No	271 (47.19%)	2,065 (56.84%)	1,061 (59.60%)	66 (68.02%)	
Yes	229 (52.81%)	1,654 (43.16%)	790 (40.40%)	45 (31.98%)	
Diabetes					0.158
No	402 (84.50%)	3,033 (86.69%)	1,560 (88.81%)	99 (91.28%)	
Yes	98 (15.50%)	686 (13.31%)	291 (11.19%)	12 (8.72%)	
Smoke_status					0.244
No	306 (59.01%)	2,312 (60.73%)	1,219 (64.77%)	72 (63.03%)	

Table 2 (continued)

Characteristic	Q1(0–2) *N* = 500	Q2(3–5) *N* = 3,719	Q3(6–8) *N* = 1,851	Q4(9–11) *N* = 111	*p*-value
Yes	194 (40.99%)	1,407 (39.27%)	632 (35.23%)	39 (36.97%)	
VMPA					0.095
No	276 (46.29%)	1,865 (45.74%)	1,016 (51.07%)	70 (59.68%)	
Yes	224 (53.71%)	1,854 (54.26%)	835 (48.93%)	41 (40.32%)	
Hypertension					0.105
No	327 (73.46%)	2,325 (67.70%)	1,186 (69.93%)	77 (79.38%)	
Yes	173 (26.54%)	1,394 (32.30%)	665 (30.07%)	34 (20.62%)	
Liver fibrosis					0.003
No	433 (82.48%)	3,327 (90.96%)	1,685 (92.79%)	104 (93.22%)	
Yes	67 (17.52%)	392 (9.04%)	166 (7.21%)	7 (6.78%)	

Note Categorical variables are presented as unweighted frequencies and weighted percentages, and group comparisons are performed using weighted chi-square tests. Continuous variables are presented as weighted means ± standard deviations, and group comparisons are performed using weighted analysis of variance (ANOVA) or weighted Kruskal-Wallis tests

Table 3 Association between DI-GM quartiles and NAFLD or liver fibrosis risk

Variables	Outcome	Model 1		Model 2		Model 3	
		OR (95%CI)	*P*-value	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
NAFLD	DI-GM	0.931 (0.886,0.979)	0.007	0.914 (0.868,0.962)	0.001	0.844 (0.757,0.941)	0.004
	DI-GM (quartile)						
	Q1	1(reference)		1(reference)		1(reference)	
	Q2	0.678 (0.51,0.903)	0.01	0.635 (0.47,0.859)	0.006	0.628 (0.432,0.913)	0.024
	Q3	0.606 (0.431,0.851)	0.006	0.532 (0.372,0.759)	0.002	0.538 (0.341,0.848)	0.017
	Q4	0.42 (0.219,0.806)	0.011	0.416 (0.209,0.828)	0.016	0.42 (0.187,0.946)	0.041
	P for trend		0.006		0.002		0.018
Liver Fibrosis	DI-GM	0.844 (0.757,0.941)	0.004	0.83 (0.74,0.931)	0.003	0.861 (0.746,0.993)	0.043
	DI-GM (quartile)						
	Q1	1(reference)		1(reference)		1(reference)	
	Q2	0.468 (0.287,0.761)	0.004	0.441 (0.268,0.725)	0.003	0.458 (0.247,0.247)	0.022
	Q3	0.366 (0.191,0.7)	0.004	0.327 (0.164,0.653)	0.003	0.367 (0.159,0.159)	0.027
	Q4	0.343 (0.088,1.328)	0.115	0.34 (0.082,1.409)	0.127	0.408 (0.074,0.074)	0.236
	P for trend		0.013		0.011		0.045

Note Model 1: Unadjusted; Model 2: Adjusted for gender, age, and race; Model 3: Adjusted for gender, age, race, education level, marital status, PIR, V/MPA, hypertension, diabetes, smoking, protein, carbohydrate, total sugars, dietary fiber, total fat, BMI, WC, BP, TC, TG, HDL-C, LDL-C, HbA1c, and INS

NAFLD [22–24]. Additionally, other studies have shown that the gut microbiome can either ameliorate or exacerbate NAFLD progression through multiple mechanisms, such as altering gut permeability, regulating energy absorption from the diet, influencing hepatic lipogenesis, modulating the expression of genes involved in choline and bile acid metabolism pathways, and even interacting with innate immunity through the production of ethanol in the gut [25].

This study found that higher DI-GM scores are associated with a lower risk of NAFLD or liver fibrosis, which may reflect the effect of dietary components in modulating the gut microbiome and influencing the production of these metabolic products [26]. The DI-GM score combines the intake of beneficial foods (such as fermented dairy products and whole grains) and harmful foods (such as red meat and refined grains), indirectly affecting the composition of the gut microbiome and subsequently influencing the production of beneficial metabolites like SCFAs. Previous studies have shown that dietary patterns rich in fiber, prebiotics, and a diverse range of plant-based foods help promote SCFA production, while diets high in fat, sugar, and meat promote the production of harmful metabolites, leading to gut microbiome imbalance and an increased risk of NAFLD [27–29]. Moreover, the gut microbiome not only regulates hepatic fat metabolism via its metabolites but also plays a significant role in hepatic inflammation [30]. The onset of NAFLD is closely associated not only with fat deposition but also with chronic low-grade inflammation. Studies have shown that secondary bile acids activate the farnesoid X receptor (FXR) in the liver, regulating fat metabolism and inhibiting liver inflammation [31]. However, excessive secondary bile acids may worsen fat deposition and trigger steatohepatitis, thereby accelerating the progression of NAFLD [32]. These findings suggest that dietary patterns, by regulating the gut microbiome and influencing the production of these metabolic products, may

Variable	Count	Percent	P_value	OR	Lower	Upper	P for interaction
Overall	6181	100	0.068	0.97	0.94	1	
Sex							0.248
Male	2797	45.3	0.875	1	0.95	1.04	
Female	3384	54.7	0.06	0.96	0.92	1	
Race							0.058
Mexican American	717	11.6	0.822	1.01	0.92	1.11	
Other Hispanic	632	10.2	0.689	0.98	0.89	1.08	
Non-Hispanic White	2135	34.5	<0.001	0.91	0.87	0.96	
Non-Hispanic Black	1651	26.7	0.2	0.96	0.9	1.02	
Other Race	1046	16.9	0.422	1.03	0.96	1.1	
Education							0.301
Less than high school	1027	16.6	0.431	1.03	0.95	1.12	
High schoolor GED	1433	23.2	0.67	0.99	0.92	1.05	
College or above	3721	60.2	0.057	0.96	0.93	1	
Marital_status							0.709
Never married	1236	20	0.058	0.93	0.87	1	
Married or living with partner	3602	58.3	0.075	0.97	0.93	1	
Widowed or divorced	1343	21.7	0.252	0.96	0.9	1.03	
PIR							0.426
<1.30	1414	22.9	0.806	1.01	0.94	1.08	
1.30-3.49	2868	46.4	0.189	0.97	0.93	1.01	
≥3.50	1899	30.7	0.073	0.95	0.9	1	
BMI							0.244
<25	1547	25	0.022	1.11	1.01	1.2	
25-30	1999	32.3	0.247	1.03	0.98	1.09	
≥30	2635	42.6	0.54	1.02	0.97	1.07	
Diabetes							0.638
No	5094	82.4	0.226	0.98	0.95	1.01	
Yes	1087	17.6	0.992	1	0.93	1.08	
Smoke_status							0.904
No	3909	63.2	0.151	0.97	0.94	1.01	
Yes	2272	36.8	0.355	0.98	0.93	1.03	
VMPA							0.857
No	3227	52.2	0.222	0.98	0.94	1.02	
Yes	2954	47.8	0.179	0.97	0.93	1.01	
Hypertension							0.705
No	3915	63.3	0.249	0.98	0.94	1.02	
Yes	2266	36.7	0.175	0.97	0.92	1.02	

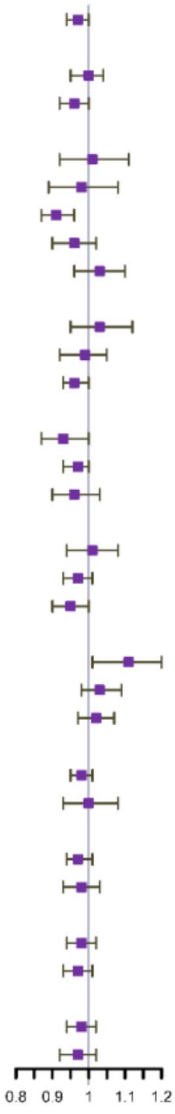

Fig. 2 Subgroup analysis forest plot

be an important mechanism underlying the association between higher DI-GM scores and lower NAFLD or liver fibrosis risk in this study.

In addition to directly affecting the composition of the microbiome, diet al.so modulates the interaction between the gut and liver through the gut-liver axis, thereby influencing the development and progression of NAFLD [33]. The gut-liver axis modulates the metabolic state of the liver through multiple pathways, including microbial metabolites, gut barrier function, and immune responses. The metabolic products of the gut microbiome, such as SCFAs, bile acids, TMA, and its derivative TMAO, enter the liver via the gut-liver axis, influencing liver fat metabolism, insulin sensitivity, and inflammation, thus playing an essential role in the onset and progression of NAFLD [34, 35]. For example, SCFAs promote gut barrier function, reducing the translocation of harmful substances, enhancing insulin sensitivity, and inhibiting hepatic fat accumulation [28]. Furthermore, SCFAs can activate GPR41 and GPR43 receptors, further regulating hepatic fatty acid metabolism and oxidation processes, thereby inhibiting the progression of fatty liver [36]. Bile acids play a key role in the pathogenesis of NAFLD by activating the FXR receptor, which regulates hepatic lipid metabolism, insulin signaling pathways, and feedback mechanisms [37, 38]. However, excessive accumulation of bile acids may exacerbate NAFLD progression by further activating liver inflammation [39]. Trimethylamine-N-oxide (TMAO), a metabolic product of the gut microbiome, has been shown to significantly impact the onset and progression of NAFLD by

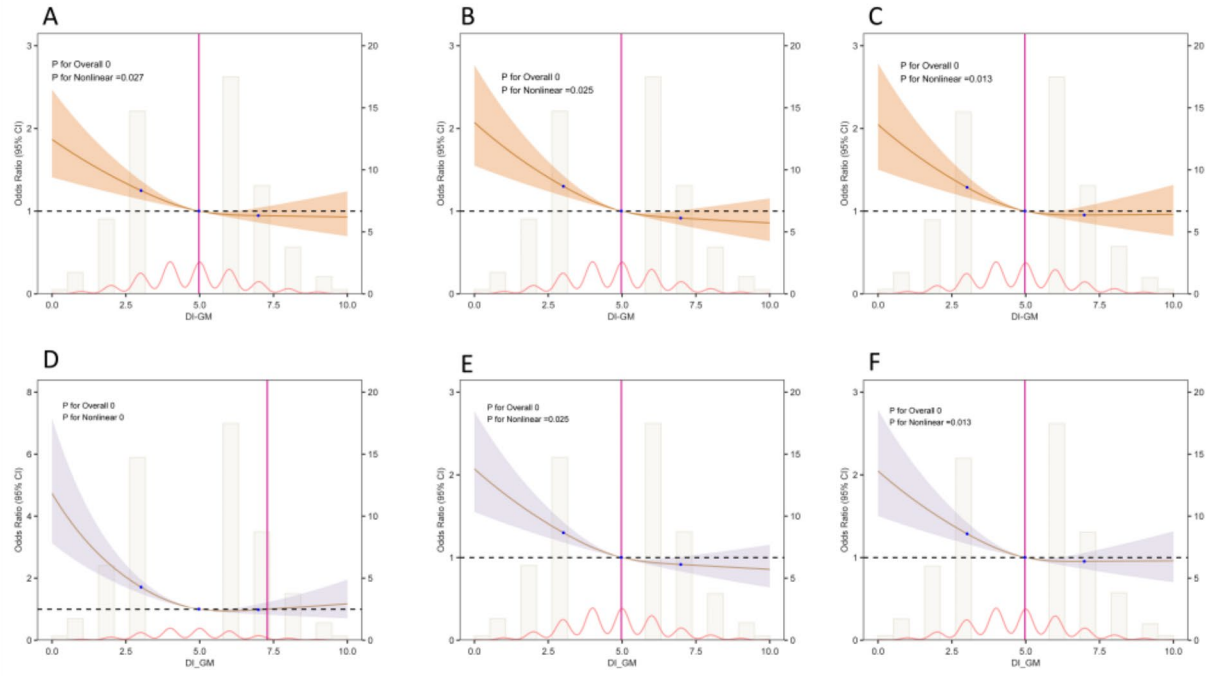

Fig. 3 Restricted cubic spline (RCS) analysis of the relationship between DI-GM and the risk of NAFLD or liver fibrosis across different models. Panels **A**-**C** represent NAFLD, while Panels **D**-**F** represent liver fibrosis. Panel **A** and **D** show the unadjusted Model 1, Panel **B** and **E** display the partially adjusted Model 2, and Panel **C** and **F** depict the fully adjusted Model 3

promoting hepatic fat synthesis and oxidation, as well as intensifying systemic inflammation [21, 40].

Moreover, Dysbiosis of the gut microbiome may also compromise the integrity of the gut barrier, facilitating the entry of endotoxins (such as lipopolysaccharides, LPS) into the bloodstream, triggering hepatic immune responses, and further promoting liver fat accumulation and chronic inflammation [41]. Dietary patterns, by influencing the composition of the gut microbiome, may enhance gut barrier function, reduce the transfer of harmful substances to the liver, and thereby reduce hepatic inflammation and the risk of NAFLD [42]. Studies have shown that dietary patterns rich in fiber, fermented foods, and plant-based foods can significantly increase the diversity of the gut microbiome, which helps maintain gut barrier integrity and reduce intestinal inflammation [43, 44]. For example, the intake of dietary fibers and prebiotics promotes the proliferation of beneficial bacteria, such as Bifidobacterium and Lactobacillus, improving the gut microbiota balance [45]. This, in turn, enhances gut barrier function, reduces the translocation of lipopolysaccharides (LPS), and subsequently lowers the risk of NAFLD onset and progression. In this study, we found that higher DI-GM scores are associated with a lower risk of NAFLD or liver fibrosis, which may be mediated by promoting gut health, improving gut barrier function, reducing the transfer of endotoxins, thereby alleviating hepatic inflammation, and ultimately lowering the risk of NAFLD or liver fibrosis. These preliminary findings provide a theoretical foundation for further exploration of the role of the gut-liver axis in NAFLD or liver fibrosis.

Moreover, in this study, we observed that higher DI-GM quartiles were associated with an increased number of individuals who were female, Non-Hispanic White, had higher education levels, were married or cohabiting, and had an income level ≥ 3.50. This may reflect that these groups are more inclined to adopt healthier dietary patterns, particularly individuals with higher education and higher income who are more likely to choose diets that promote gut health [46]. However, despite the differences in DI-GM distribution across these groups, subgroup analysis did not show significant interactions. One possible explanation is that, although DI-GM is associated with health behaviors in these groups, its relationship with NAFLD may not be significantly influenced by these socio-economic factors. Future research should further investigate the role of factors such as gender and cultural background in the relationship between DI-GM and metabolic diseases, while better controlling for potential confounders to reveal specific mechanisms in different groups.

Despite being based on the NHANES database, with a large sample size and good national representativeness, which enhances the external validity and robustness of the results, this study still has some limitations. First, this study employed a cross-sectional design, which limits the ability to infer causal relationships. Although we observed a negative association between higher DI-GM scores and NAFLD risk, this finding cannot exclude the potential influence of confounding factors, and thus the causal relationship between DI-GM and NAFLD cannot be definitively established. Future longitudinal studies could provide a better understanding of the causal relationship between DI-GM and NAFLD risk. Secondly, although the DI-GM score accounts for the influence of 14 foods or nutrients, it may not fully capture the complex impacts of all dietary factors on the gut microbiome, especially the effects of other dietary components, such as trace elements and specific fatty acids, which have not been sufficiently considered. Therefore, future research may explore the effects of different dietary patterns on the gut microbiome using more advanced dietary assessment tools. Finally, although the data in this study are derived from the U.S. population, which has strong external representativeness, the findings may not be fully applicable to populations from other races or regions, particularly when there are significant differences in dietary culture and genetic backgrounds. Therefore, future studies should be carried out in populations from various races and regions to validate the generalizability and regional differences of the conclusions.

Conclusions

This study indicates that higher DI-GM scores are inversely associated with lower NAFLD risk or liver fibrosis, suggesting that healthy dietary patterns may reduce the risk of NAFLD or liver fibrosis by improving the composition of the gut microbiome. This provides a theoretical foundation for dietary intervention-based NAFLD or liver fibrosis prevention strategies, emphasizing the potential role of dietary patterns in the prevention and management of metabolic diseases.

Abbreviations

DI-GM	Dietary Index for Gut Microbiota
NAFLD	Non-Alcoholic Fatty Liver Disease
NHANES	National Health and Nutrition Examination Survey
CAP	Controlled Attenuation Parameter
PIR	Family Income and Poverty Ratio
BMI	Body Mass Index
WC	Waist Circumference
BP	Blood Pressure
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
TG	Triglyceride
TC	Total Cholesterol
HDL-C	High-Density Lipoprotein
LDL-C	Low-Density Lipoprotein Cholesterol
HbA1c	Glycohemoglobin
INS	Insulin
FPG	Fasting Plasma Glucose
V/MPA	Physical Activity

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Author contributions

C.Z.:Writing original draft; Writing-review&editing;Methodology;Data analysis and visualization. Z.Q.:Writing original draft; Writing-review&editing;Methodology; R.C.:Writing-review&editing;Data analysis. Z.L.:Data analysis; Visualization. L.X.:Methodology; Validation; Writing-review; F.Z.:Funding acquisition; supervision. All authors approved the manuscript and agreed to publish.

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Data availability

All datasets provided in this study are derived from the National Health and Nutrition Examination Survey (NHANES) and are accessible on the NHANES official website at https://wwwn.cdc.gov/nchs/nhanes/Default.aspx.

Declarations

Ethics approval and consent to participate

This study used publicly available summary data, and ethics approval was not necessary.

Informed consent

Written informed consent was obtained from all participants in the study.

Competing interests

The authors declare no competing interests.

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