



OPEN The mediating role of inflammatory factors in the association between dietary index for gut microbiota and hypertension

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Hypertension is a major global health concern, closely linked to cardiovascular, renal, and cerebrovascular diseases. This study investigates the relationship between the dietary index for gut microbiota (DI-GM) and hypertension, focusing on the role of inflammatory factors as mediators. We analyzed data from 21,212 participants in the NHANES 2007–2018 dataset. The results show that higher DI-GM scores are significantly associated with a reduced risk of hypertension, particularly systolic blood pressure. Mediation analysis further reveals that inflammatory factors—specifically white blood cell count, neutrophils, and systemic inflammatory index (SII)—partially mediate this relationship. The mediating effects of white blood cell count, neutrophils, and SII account for 9.07%, 8.64%, and 3.97% of the total effect, respectively. These findings suggest that dietary patterns associated with gut microbiota health are inversely related to hypertension risk, and this association may be partially explained by systemic inflammation. This study highlights the potential of diet as a non-pharmacological strategy for managing hypertension and emphasizes the importance of gut microbiota in blood pressure regulation. Our results provide new insights into the complex interactions between diet, gut health, inflammation, and blood pressure control, suggesting that dietary modifications could be a key intervention in hypertension prevention and management.

Keywords Dietary index for gut microbiota (DI-GM), Hypertension, NHANES, Mediation

Abbreviations

DI-GM	Dietary index for gut microbiota
NHANES	National Health and Nutrition Examination Survey
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
RCS	Restricted cubic spline
WBC	White blood cell count
NEU	Neutrophils
SII	Systemic inflammatory index
DASH	Dietary approaches to stop hypertension
SCFAs	Short-chain fatty acids
BMI	Body mass index
PIR	Poverty income ratio
CVD	Cardiovascular disease
DM	Diabetes mellitus
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance

Hypertension, a globally prevalent condition closely associated with vascular, cardiac, renal, and cerebrovascular diseases, significantly contributes to global mortality and imposes a substantial public health burden¹. Projections suggest that the global prevalence of hypertension will decline to 20.3% by 2040². However, another

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study estimates that by 2025, the global hypertensive population will increase by 60% to reach 1.56 billion³. This trend underscores the significant challenge in preventing and managing hypertension globally.

A growing number of studies have found an independent and significant association between sleep disorders⁴, particularly insufficient hours of sleep, and hypertension. Sleep deprivation (less than 6 h) elevates the risk of hypertension by inducing metabolic disorders and inflammatory responses through mechanisms such as activation of sympathetic nerves, elevated cortisol levels, and increased energy intake. In addition, poor sleep quality may also lead to dysregulation of gut flora, which in turn affects inflammation and blood pressure regulation, suggesting that the sleep-gut-blood pressure regulatory axis deserves further attention.

Diet and lifestyle play critical roles in the development and management of hypertension. Excessive intake of salt, fat, and sugar promotes the onset of hypertension⁵, whereas healthy dietary patterns such as the DASH and Mediterranean diets have been shown to lower systolic and diastolic blood pressure and reduce cardiovascular risk^{6,7}. Increasing evidence suggests that these effects are not only direct but also mediated through changes in the gut microbiota^{8,9}. For instance, dietary fiber can increase the abundance of beneficial bacteria like *Prevotella*, while polyphenols promote probiotics and reduce pathogenic species^{10–12}. In contrast, diets rich in red and processed meats may damage the gut barrier and trigger systemic inflammation¹³. These inflammatory responses—along with microbial metabolites like short-chain fatty acids (SCFAs) and trimethylamine N-oxide (TMAO)—may modulate vascular tone, immune response, and endocrine function, ultimately affecting blood pressure regulation^{14–16}.

Among non-pharmacological interventions, diet is widely recognized as an important factor in blood pressure regulation. For example, DASH diet and Mediterranean diet have been shown to have significant antihypertensive effects. However, recent studies have further pointed out that diet not only acts directly on blood pressure, but also achieves its vasoprotective effects by influencing intestinal microecology. Gut flora is a key intermediary linking diet and blood pressure: a beneficial diet promotes the production of short-chain fatty acids (SCFAs), inhibits inflammation, and enhances vasodilatation, whereas a diet high in salt and fat induces dysbiosis in the gut flora and increases harmful metabolites, such as TMAO^{17,18}. Recent studies have shown that gut flora can regulate blood pressure through multiple mechanisms¹⁷: including inflammatory pathways (e.g., NF- κ B, IL-6-mediated), neuroendocrine regulation (sympathetic excitation), and steroid hormone metabolism (corticosterone synthesis). Diet has an important impact on blood pressure levels by influencing the composition of the gut flora, which in turn affects the degree of activation of these pathways.

Numerous studies demonstrate that the gut microbiota can influence blood pressure, suggesting that regulating the gut microbiota profile will lead to blood pressure control^{19,20}. The Dietary Index for Gut Microbiota (DI-GM) is a recently proposed tool for assessing the effect of diet on gut microbiota²¹. The DI-GM includes a total of 14 foods or nutrients that have a beneficial and a detrimental impact of gut microbial characteristics. Beneficial ingredients include 10 ingredients such as green tea, coffee, dietary fiber, and broccoli, and unfavorable ingredients include 4 ingredients such as refined grains and processed meats. The DI-GM was selected through a systematic review of the literature and was able to accurately incorporate foods that directly improve or maintain the health of the gut microbiota. Compared to other dietary indices (e.g., HEI, MDS), the DI-GM includes well-defined foods (e.g., broccoli, avocado, etc.), which is a combination of 14 foods that accurately assesses the quality of the diet related to gut health. Previous studies have demonstrated that DI-GM correlates well with intestinal flora diversity and metabolites; however, its association with hypertension lacks direct epidemiologic study support. The 14 food items included in the DI-GM were selected based on a systematic literature review focused on dietary influences on gut microbiota composition and function²¹. Unlike broader indices such as the Healthy Eating Index (HEI) or the Dietary Approaches to Stop Hypertension (DASH), which evaluate overall diet quality or cardiovascular health outcomes, DI-GM specifically incorporates foods with documented impacts on microbiome diversity and metabolite production. This targeted design allows for a more mechanistic interpretation of the diet-hypertension relationship through the lens of microbiota-mediated inflammation.

Therefore, the present study, based on data from the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2018, aimed to explore the association between DI-GM and hypertension and to further analyze the mediating role of inflammatory factors in it. This study intends to fill in the still unclear link in the diet-gut flora-inflammation-hypertension chain and enrich the evidence of cross-cutting studies in microecological nutrition and cardiovascular epidemiology.

Methods

Study population

The National Health and Nutrition Examination Survey (NHANES) is organized and conducted by the National Center for Health Statistics (NCHS), part of the Centers for Disease Control and Prevention (CDC), and is designed to collect data on the health and nutritional status of the population through a nationally representative sample. This ongoing cross-sectional survey is conducted every two years and uses stratified multistage probability sampling methods to ensure that it is representative of the non-incarcerated civilian population of the United States. Participants are interviewed with questionnaires at home and undergo detailed physical examinations and laboratory tests at an ambulatory screening center. Seven data cycles between 2007 and 2018 were used in this study to ensure broad data coverage. All participants provided informed consent prior to the start of the survey, and data collection and study methods were approved by the NCHS Ethics Review Board. A detailed description of the methods can be found on the official CDC website (<https://www.cdc.gov/nchs/nhanes.htm>).

We analyzed the 2007–2018 population in the NHANES database with the following exclusions among the initial 59,842: DI-GM, hypertension missing values ($n = 19163$), age ≤ 20 years ($n = 11325$), demographic data (e.g., PIR, alcohol consumption, smoking status, marital status, education) missing values ($n = 4745$), missing values for other diseases (e.g., CVD, DM) ($n = 251$), missing values for inflammatory factors ($n = 832$) and

tumors, as well as patients who were pregnant ($n=2314$); ultimately, 21,212 participants were included in the present study, and details of the exclusion from inclusion are shown in Fig. 1.

Diagnosis of hypertension

For the purpose of this study, the definition of hypertension followed the standards of the American Heart Association and the International Society of Hypertension. The professional examiners of the NHANES team measured the blood pressure of the participants according to the norms, which can be found on the official website of NHANES (<https://www.cdc.gov/nchs/nhanes.htm>). After a 5-minute quiet rest, each participant's blood pressure was measured three times consecutively in a relaxed state. The average blood pressure values (systolic and diastolic) were calculated following a standardized protocol: diastolic blood pressure (DBP) readings of zero were excluded from the calculation, and if all DBP readings were zero, the average was set to zero. When only one blood pressure reading was available, that single reading was used as the average. In cases where multiple readings were recorded, the first reading was excluded, and the average was computed using the remaining measurements. Criteria for determining hypertension included (1) mean systolic blood pressure (SBP) ≥ 140 mmHg; (2) mean diastolic blood pressure (DBP) ≥ 90 mmHg; (3) self-reported diagnosis of hypertension; or (4) taking antihypertensive medication²². This multiple-measurement averaging method improves the accuracy of blood pressure data and is widely used in epidemiologic studies to ensure the reliability of hypertension prevalence assessments.

Dietary index for gut microbiota (DI-GM) evaluation

Based on the Kase et al. scale²¹, the DI-GM includes 14 foods and nutrients that are categorized as beneficial or unfavorable based on their potential impact on the gut microbiota. Beneficial ingredients included fermented dairy products, chickpeas, soy, whole grains, dietary fiber, cranberries, avocado, broccoli, coffee, and green tea, all of which were considered likely to have a positive impact on gut health. Unfavorable ingredients, on the other hand, include red meat, processed meats, refined grains, and high-fat diets ($\geq 40\%$ of energy provided by fat), which may negatively impact the gut microbiota. DI-GM scores were calculated based on NHANES dietary

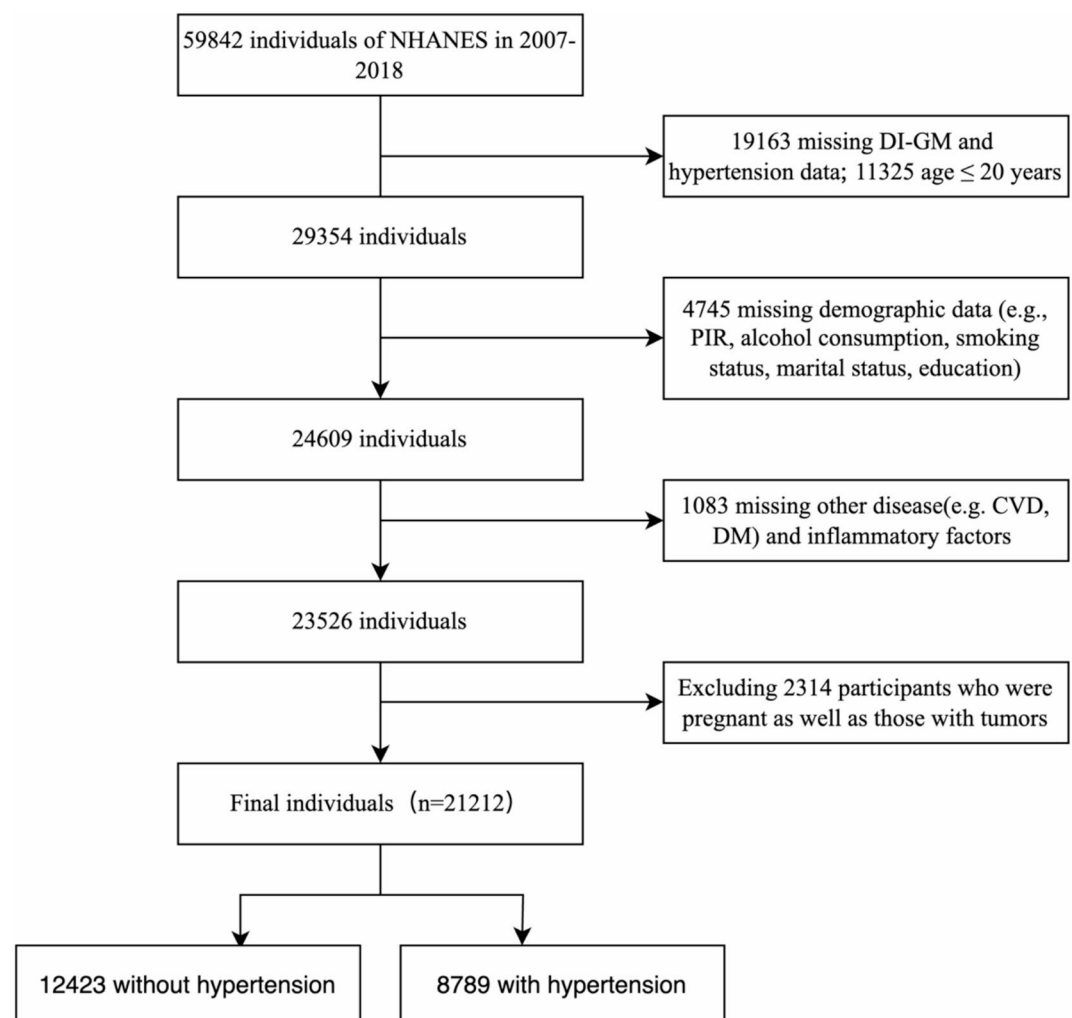


Fig. 1. Inclusion exclusion flowchart for this study.

recall data from 2007 to 2018, and the specific scoring criteria as well as the components are shown in Table S1. Scoring was based on the sex-specific median: 1 point was assigned if beneficial ingredient intake was at or above the median and 0 points otherwise; for unfavorable components, 1 point if intake is below the median and 0 points otherwise. All 14 components in the DI-GM were equally weighted, with each assigned 1 point based on sex-specific median intake thresholds. Avocado was included not solely for its fiber content but for its consistent and multidimensional impact on gut microbiota, including SCFA production, microbial diversity, and epithelial barrier integrity. This decision was supported by multiple human studies showing that avocado intake increased the abundance of beneficial taxa (e.g., *Faecalibacterium*, *Prevotellaceae*) and enhanced fecal SCFA concentrations. Higher DI-GM scores represent dietary patterns that are potentially more beneficial to the gut microbiota. In addition, DI-GM scores were further grouped into 0–3, 4, 5, and ≥ 6 , and also categorized into favorable (0–10) and unfavorable (0–4) dietary patterns based on microbiota-modulating potential.

Covariates and leukocytes, neutrophils, SII

We selected a variety of variables to ensure the accuracy of our results, including: age, sex, race, marital status, education, PIR, smoking, and drinking status, similar to published articles²³. For age, we further categorized into < 60 , ≥ 60 ; race included Non-Hispanic White, Non-Hispanic Black, Mexican American, and Other Race; and education was categorized as Less than 12th grade, High school or Smoking status was obtained through questionnaires asking “Have smoked at least 100 cigarettes in your life” and “Do you smoke now? Do you smoke now?”, categorized as Never, Ever, and Current. For categorization of alcohol use we used a similar methodology to that study²⁴: never drinkers (< 12 drinks/lifetime); ex-drinkers (≥ 12 drinks in 1 year and no drinks in the past 1 year, or ≥ 12 drinks in lifetime but no drinks in the past 1 year). (≥ 12 drinks in 1 year, no drinks in the past 1 year, or ≥ 12 drinks in lifetime but no drinks in the past 1 year). Light drinking: women = 1 time, men = 2 times; moderate drinking: women = 2 times, men = 3 times, or intermittent drinking ($2 \leq \text{binge} < 5$); heavy drinking: women = 3 times, men = 4 times, or intermittent drinking ($\text{binge} \geq 5$). Participants’ marital status was categorized as Never married, Married or cohabitation, Widowed or separated, coronary heart disease (yes/no), DM (yes/no). Body mass index (BMI, kg/m²) was categorized as ($< 24/\geq 24$). Blood specimens were collected for measurement after 8 h of fasting. SII was defined as platelet count multiplied by neutrophil count/lymphocyte count in 103 cells/mL²⁵. Since classical inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) are not available in NHANES, we selected white blood cell (WBC) count, neutrophil (NEU) count, and the systemic immune-inflammation index (SII) as surrogate markers. These variables are widely used in epidemiological studies as accessible and representative proxies for systemic inflammation. Notably, a recent NHANES-based study using data from 1999 to 2018, demonstrated that higher SII levels were significantly associated with increased risks of all-cause and cardiovascular mortality in individuals with type 2 diabetes, further supporting its validity as a population-based biomarker of chronic systemic inflammation²⁶.

Statistical analysis

Complex sampling and weighted analyses were used in this study according to the NHANES study guidelines. Baseline characteristics of participants with and without hypertension were described. Continuous variables were expressed as means and standard deviations (SD), while categorical variables were expressed as counts and percentages. Sex differences within hypertension groups were tested using weighted t-tests for continuous variables and weighted chi-square tests for categorical variables. To better present sex-based differences, Supplementary Table 2 was split into Table 2A (non-hypertensive) and Table 2B (hypertensive), and Supplementary Table 3 into Table 3A (non-hypertensive) and Table 3B (hypertensive). These tables show sex-specific comparisons using weighted t-tests for continuous variables and chi-square tests for categorical variables. To address missing data, a multiple filling method was used to minimize potential effects on the study results. To assess the association between DI-GM and hypertension and its components (systolic SBP and diastolic DBP), three multivariate weighted regression models were constructed: model 1 was unadjusted; model 2 adjusted for age, sex, and ethnicity; model 3 further included education level, poverty-to-income ratio (PIR), smoking and drinking status, BMI, and history of cardiovascular disease (CVD). These covariates were selected a priori based on their established associations with both dietary patterns and blood pressure outcomes, supported by previous NHANES-based and cardiovascular epidemiology studies. Given that DI-GM is a continuous variable and its association with hypertension risk may not be linear, this study used Restricted Cubic Spline (RCS) for modeling and analysis. RCS, which has the characteristics of flexible modeling and high fitting accuracy, is commonly used in nutritional epidemiology to reveal nonlinear associations between exposure variables and outcomes. In addition, we analyzed the association of DI-GM with overall risk of hypertension, systolic blood pressure (SBP) and diastolic blood pressure (DBP) separately using RCS to explore the potential differences in different blood pressure indicators. As SBP and DBP have different physiological regulatory mechanisms, modeling them separately helps to more precisely assess the role characteristics of DI-GM. Stratified analyses were used to explore the stability and interaction of the relationship between DI-GM and hypertension under different population characteristics (e.g., age, race, marital status, education level, BMI, smoking, alcohol consumption, CVD, and diabetes). In addition, to assess the mediating role of inflammatory factors in the relationship between DI-GM and hypertension, mediation effect analysis was performed, and the selected metrics included white blood cell count (WBC), neutrophils (NEU), and systemic inflammatory index (SII). Mediation analyses were performed using the Sobel test, Bootstrap method, and quasi-Bayesian Monte Carlo simulations based on normal approximation (500 iterations), implemented using the “mediation” package of R. The mediation analysis was performed using the Sobel test, Bootstrap method, and quasi-Bayesian Monte Carlo simulations based on normal approximation (500 iterations). All mediation models were adjusted for a consistent set of potential confounders, including age, sex, ethnicity, BMI, education level, PIR, smoking and drinking status, and history of cardiovascular disease. These variables were selected based on prior literature and their known

relevance to both dietary patterns and hypertension risk. To ensure consistency and reduce overfitting, a fixed set of covariates was used across all models, and no stepwise selection or data-driven filtering was applied. To ensure methodological consistency, we applied the same covariate structure across both the primary regression and mediation models. Although the cross-sectional design of this study does not allow for a clear temporal causality between variables, mediation analyses can still provide exploratory insights into underlying biological mechanisms. All analyses were performed using R software (version 4.4.1; <https://www.R-project.org/>) with the “survey” package for weighted analyses, the “mice” package for multiple imputation, and the “mediation” package for mediation analyses. The level of statistical significance was set at a two-sided p -value < 0.05 .

Results

Characteristics of participants in this study

A total of 21,212 participants from NHANES (2007–2018) were included in this study. Among these participants, approximately 8,780 (41.4%) were hypertensive. Approximately half of the participants were male ($n = 10,643$; 50.05%), with 67.59% identifying as non-Hispanic White, and the mean age was 46.29 years. Table 1 demonstrates the detailed baseline data comparison. It is clear from the table that patients with hypertension were usually older (mean age 55.27 vs. 41.12 years, $p < 0.0001$), more likely to be male ($p = 0.01$), less educated ($p < 0.0001$), and had lower income (PIR: 2.96 vs. 3.07, $p = 0.002$). Smoking ($p < 0.0001$) and drinking habits ($p < 0.0001$) also differed significantly between the two groups. In addition, for our derived DI-GM, there was also a significant difference between the two groups: the DI-GM was lower in hypertensive patients (4.62 vs. 4.74, $p < 0.001$). Inflammatory markers, including WBC (7.42 vs. 7.12), neutrophils (4.43 vs. 4.19), and SII (553.65 vs. 513.07), were all significantly elevated in hypertensive patients compared to their non-hypertensive counterparts (all $p < 0.0001$). Table S2 provides a baseline characterization of participants stratified by gender and hypertension status. To further illustrate sex-specific differences, Supplementary Table S2 was subdivided into Table S2A (non-hypertensive participants) and Table S2B (hypertensive participants), each stratified by sex. Supplementary Table S3 was likewise divided into Table S3A and Table S3B to show the distribution of DI-GM components by sex within each hypertension group. These tables provide detailed comparisons, with corresponding p -values indicating significant differences between males and females in each group. In Table S3 we performed a baseline characterization of the specific composition of the DI-GM according to gender and the presence of hypertension. Table S4 further excluded those using hypoglycemic, antihypertensive, and lipid-lowering medications from the included population, resulting in the inclusion of 13,679 participants.

Association between DI-GM and hypertension

Table 2 demonstrates the relationship between DI-GM and hypertension. A unit increase in DI-GM was associated with a 4% reduction in hypertension risk ($p < 0.001$), a 30% reduction in systolic blood pressure ($p = 0.003$), and a 12% reduction in diastolic blood pressure ($p = 0.02$). After adjusting for a variety of variables, the risk of hypertension could be reduced by 8% ($p < 0.001$) and the reduction in systolic as well as diastolic blood pressure remained significant. After grouping DI-GM and adjusting for multiple covariates, those with $\text{DI-GM} \geq 6$ could significantly reduce the risk of hypertension (OR = 0.79, 95%CI = 0.71, 0.88), although statistical significance for reductions in systolic and diastolic blood pressure was not observed. An increase in beneficial intestinal bacteria was associated with a decrease in hypertension risk and systolic blood pressure, whereas no significant effect was observed for diastolic blood pressure. No significant association was observed between unfavorable gut microbiota and hypertension as well as its composition after adjusting for multiple variables. Sensitivity analysis, excluding individuals using hypoglycemic, antihypertensive, and lipid-lowering medications, confirmed that higher DI-GM scores were consistently associated with lower hypertension incidence ($p < 0.001$).

To assess the stability of the relationship between DI-GM and hypertension, we performed subgroup analyses (Table 3). As can be seen from the table, the relationship between DI-GM and hypertension was not meaningful in most subgroups. This suggests that marital status (Never married/Married or cohabitation/Widowed or separated), education (Less than 12th grade/High school or equivalent/college graduate or above), BMI ($< 24/\geq 24$), smoke (Never/Ever/Current), alcohol (never/ former/ mild/ moderate/ heavy), CVD (no/yes), and DM (no/DM/IFG/IGT) have no significant effect on the correlation between the two is no significant effect. However, there was a significant interaction between DI-GM and hypertension in age and race stratification ($p < 0.001$). The nonlinear relationships between DI-GM as a continuous variable and beneficial and non-beneficial gut microbiota on hypertension as well as systolic and diastolic blood pressure, respectively, are shown in Table 2. Figure 2 clearly demonstrates that higher DI-GM scores are associated with lower risk of developing hypertension, and a similar relationship can be seen in systolic and diastolic blood pressure, and all show a nonlinear relationship (p for nonlinear > 0.05).

Role of inflammatory factors in DI-GM in hypertension

Furthermore, Fig. 3 clearly demonstrates that after modulation of multiple variables, DI-GM was found to have both direct effects on hypertension and indirect effects mediated through inflammatory factors. The indirect effect of DI-GM on the incidence of hypertension through WBC was 9.07%; Neutrophils accounted for 8.64% of the total effect; and the indirect effect of SII was lesser at 3.97%. It is easy to see that WBC and Neutrophils play a mediating role in the development of hypertension by DI-GM, while SII has a smaller effect than the other two.

Discussion

In this study, DI-GM was analyzed as a continuous and categorical variable, and an in-depth analysis of data from 21,212 NHANES revealed a significant association between DI-GM and hypertension. The results showed a negative linear association between DI-GM and hypertension, suggesting that higher DI-GM scores are

Variable	Total	Without Hypertension	Hypertension	P value
Age(years)	46.29 ± 0.25	41.12 ± 0.25	55.27 ± 0.23	< 0.0001
Sex				0.01
Male	10,643(50.05)	6184(49.25)	4459(51.44)	
Female	10,569(49.95)	6239(50.75)	4330(48.56)	
Marital				< 0.0001
Never married	3879(18.17)	2883(22.38)	996(10.85)	
Married or cohabitation	12,804(64.42)	7631(64.38)	5173(64.48)	
Widowed or separated	4529(17.41)	1909(13.24)	2620(24.67)	
Ethnicity				< 0.0001
Mexican American	3309(8.65)	2127(9.84)	1182(6.59)	
Non-Hispanic White	8870(67.59)	5207(66.99)	3663(68.63)	
Non-Hispanic Black	4424(10.68)	2130(9.09)	2294(13.46)	
Other Race	4609(13.08)	2959(14.09)	1650(11.32)	
Education				< 0.0001
Less than 12th grade	4888(14.80)	2536(13.33)	2352(17.36)	
High school or equivalent	4828(22.93)	2658(21.31)	2170(25.74)	
College graduate or above	11,496(62.27)	7229(65.36)	4267(56.89)	
PIR	3.03 ± 0.04	3.07 ± 0.04	2.96 ± 0.04	0.002
Alcohol				< 0.0001
Never	2873(10.27)	1545(9.55)	1328(11.52)	
Former	3266(12.44)	1479(9.87)	1787(16.92)	
Mild	7104(36.58)	4122(36.01)	2982(37.59)	
Moderate	3433(18.34)	2240(19.97)	1193(15.49)	
Heavy	4536(22.37)	3037(24.60)	1499(18.49)	
Smoke				< 0.0001
Never	11,806(56.24)	7301(59.00)	4505(51.44)	
Ever	4933(23.91)	2383(20.60)	2550(29.67)	
Current	4473(19.84)	2739(20.40)	1734(18.88)	
BMI (kg/m ²)	29.23 ± 0.10	27.99 ± 0.10	31.38 ± 0.11	< 0.0001
BMI(kg/m ²)				< 0.0001
<24	4604(22.55)	3438(28.16)	1166(12.77)	
≥24	16,608(77.45)	8985(71.84)	7623(87.23)	
DI- GM	4.70 ± 0.02	4.74 ± 0.03	4.62 ± 0.02	< 0.001
DI- GM group				0.01
0–3	5183(22.89)	2953(22.07)	2230(24.31)	
4	5245(23.79)	3097(23.57)	2148(24.16)	
5	4876(23.31)	2870(23.45)	2006(23.08)	
≥6	5908(30.01)	3503(30.91)	2405(28.44)	
Beneficial	2.15 ± 0.02	2.19 ± 0.02	2.09 ± 0.02	< 0.001
Unfavorable	2.55 ± 0.01	2.56 ± 0.02	2.54 ± 0.02	0.39
Systolic Average Reading(kg/m ²)	121.44 ± 0.21	114.92 ± 0.16	132.80 ± 0.33	< 0.0001
Diastolic Average Reading(kg/m ²)	71.28 ± 0.22	69.43 ± 0.21	74.50 ± 0.30	< 0.0001
WBC(10 ⁹ /L)	7.23 ± 0.03	7.12 ± 0.03	7.42 ± 0.04	< 0.0001
NEU(10 ⁹ /L)	4.28 ± 0.02	4.19 ± 0.03	4.43 ± 0.03	< 0.0001
SII(10 ⁹ /L)	527.87 ± 3.80	513.07 ± 3.95	553.65 ± 5.77	< 0.0001

Table 1. Baseline information on hypertensive and non-hypertensive populations in the Nhanes. Data presented as mean ± SD, n (%). All data, both continuous and categorical, are weighted. PIR, Poverty income ratio; bmi, body mass index; DI-GM, the dietary index for gut microbiota; WBC, white blood cell; NEU, neutrophil; SII, the systemic immunity-inflammation index.

strongly associated with a reduced risk of developing hypertension. This trend persisted as significant even after adjusting for multiple confounding variables. In addition, the robustness of the findings was verified by various methods, including multiple interpolation, stratified analysis, and sensitivity analysis. In this study, we analyzed the associations between DI-GM and specific blood pressure components. While DI-GM demonstrated a consistent and statistically significant inverse association with systolic blood pressure (SBP), the relationship with diastolic blood pressure (DBP) was less robust across models. This discrepancy may stem from the fact that

Character	Crude model		Model 1		Model 2	
Hypertension	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
DI_GM	0.96(0.94,0.98)	<0.001	0.90(0.88,0.92)	<0.0001	0.92(0.90,0.94)	<0.0001
DI_GM group						
0–3	ref		ref		ref	
4	0.94(0.84,1.04)	0.23	0.93(0.82,1.04)	0.20	0.98(0.87,1.10)	0.71
5	0.90(0.81,1.00)	0.04	0.79(0.70,0.90)	<0.001	0.88(0.77,1.00)	0.05
≥6	0.85(0.77,0.94)	0.001	0.65(0.59,0.73)	<0.0001	0.79(0.71,0.88)	<0.0001
p for trend (character2integer)		<0.001		<0.0001		<0.0001
Beneficial to gut microbiota	0.95(0.92,0.98)	<0.001	0.90(0.88,0.93)	<0.0001	0.93(0.91,0.96)	<0.0001
Unfavorable to gut microbiota	0.99(0.95,1.02)	0.39	0.92(0.89,0.95)	<0.0001	0.97(0.94,1.01)	0.15
Systolic average reading	β value (95% CI)	P value	β value (95% CI)	P value	β value (95% CI)	P value
DI_GM	-0.3(-0.50, -0.10)	0.003	-0.52(-0.69, -0.36)	<0.0001	-0.37(-0.54, -0.20)	<0.0001
DI_GM group						
0–3	ref		ref		ref	
4	-0.7(-1.42, 0.02)	0.06	-0.59(-1.20, 0.02)	0.06	-0.3(-0.89, 0.30)	0.32
5	-0.62(-1.41, 0.18)	0.13	-0.94(-1.67, -0.22)	0.01	-0.25(-0.98, 0.48)	0.49
≥6	-1.15(-2.05, -0.24)	0.01	-2.03(-2.81, -1.26)	<0.0001	-0.81(-1.59, -0.02)	0.05
p for trend (character2integer)		0.03		<0.0001		0.07
Beneficial to gut microbiota	-0.39(-0.62, -0.15)	0.002	-0.56(-0.75, -0.37)	<0.0001	-0.29(-0.48, -0.09)	0.004
Unfavorable to gut microbiota	-0.1(-0.37, 0.18)	0.49	-0.34(-0.60, -0.09)	0.01	-0.06(-0.30, 0.19)	0.65
Diastolic average reading	β value (95% CI)	P value	β value (95% CI)	P value	β value (95% CI)	P value
DI_GM	-0.16(-0.30, -0.03)	0.02	-0.11(-0.24, 0.03)	0.12	-0.17(-0.31, -0.04)	0.01
DI_GM group						
0–3	ref		ref		ref	
4	-0.55(-1.05, -0.06)	0.03	-0.45(-0.93, 0.04)	0.07	-0.35(-0.83, 0.14)	0.16
5	-0.24(-0.81, 0.33)	0.41	-0.06(-0.62, 0.49)	0.82	0.01(-0.56, 0.58)	0.98
≥6	-0.75(-1.35, -0.15)	0.02	-0.52(-1.11, 0.08)	0.09	-0.39(-1.00, 0.22)	0.20
p for trend (character2integer)		0.05		0.21		0.38
Beneficial to gut microbiota	-0.03(-0.19, 0.12)	0.66	0(-0.15, 0.15)	0.95	-0.07(-0.22, 0.07)	0.33
Unfavorable to gut microbiota	-0.33(-0.54, -0.12)	0.002	-0.24(-0.45, -0.03)	0.02	-0.06(-0.27, 0.15)	0.59

Table 2. Association of DI-GM with hypertension and its components systolic and diastolic blood pressure. Crude model unadjusted for covariates; Model 1 adjusted for sex, age, and race; Model 2 adjusted for smoking and drinking status, education, PIR, and CVD on the basis of model 1. The DI-GM ranges from 0–13 (including beneficial to gut microbiota [ranges from 0–9] and unfavorable to gut microbiota [ranges from 0–4]) and grouped according to 0–3, 4, 5, and ≥6. For Hypertension (binary outcome), OR (Odds Ratios) were used. For Systolic and Diastolic Blood Pressure (continuous variables), β coefficients are reported.

diastolic blood pressure is more influenced by peripheral vascular resistance and neurohumoral regulation (e.g., sympathetic nervous system activity), whereas systolic blood pressure is primarily determined by large artery stiffness and vascular compliance²⁷. This distinction has been well described in previous literature and supports our interpretation of differential responses to DI-GM. These findings offer new directions for future research to explore the variability of distinct blood pressure parameters influenced by dietary patterns. Furthermore, DI-GM may exert indirect effects on the development of hypertension through the regulation of inflammatory factors such as white blood cell count and neutrophils.

In recent years, an increasing number of studies have revealed the key role of gut flora in the development of metabolic diseases. Gut flora affects the regulatory processes of blood pressure through several mechanisms, among which the regulation of inflammatory pathways and metabolites is particularly important. First, intestinal microecological dysbiosis (dysbiosis) disrupts the intestinal barrier, resulting in bacterial metabolites

Character	95% CI	<i>p</i>	<i>p</i> for interaction
Age group			0.004
<60	0.942(0.918,0.968)	< 0.0001	
≥60	0.871(0.831,0.913)	< 0.0001	
Ethnicity			0.001
Mexican American	1.040(0.979,1.105)	0.202	
Non-Hispanic White	0.938(0.910,0.967)	< 0.0001	
Non-Hispanic Black	1.000(0.962,1.040)	0.990	
Other Race	1.015(0.961,1.072)	0.591	
Marital status			0.708
Never married	0.962(0.895,1.034)	0.293	
Married or cohabitation	0.942(0.916,0.969)	< 0.0001	
Widowed or separated	0.962(0.917,1.010)	0.116	
Education			0.392
Less than 12th grade	0.991(0.942,1.042)	0.711	
High school or equivalent	0.991(0.947,1.036)	0.679	
College graduate or above	0.962(0.936,0.989)	0.007	
BMI			0.216
<24	0.947(0.896,1.000)	0.049	
≥24	0.981(0.959,1.003)	0.091	
Smoke			0.504
Never	0.953(0.925,0.983)	0.002	
Ever	0.935(0.891,0.982)	0.008	
Current	0.975(0.929,1.024)	0.313	
Alcohol			0.465
Never	1.003(0.946,1.063)	0.920	
Former	0.938(0.884,0.995)	0.033	
Mild	0.957(0.927,0.987)	0.006	
Moderate	0.952(0.894,1.013)	0.119	
Heavy	0.932(0.887,0.978)	0.005	
CVD			0.895
No	0.957(0.937,0.978)	< 0.001	
Yes	0.952(0.865,1.047)	0.305	
DM			0.534
No	0.963(0.937,0.989)	0.006	
DM	0.983(0.926,1.043)	0.556	
IFG	1.018(0.921,1.124)	0.730	
IGT	1.027(0.899,1.172)	0.695	

Table 3. Subgroup analysis between DI-GM and hypertension. *CI* confidence interval, *DI-GM* dietary index for gut microbiota, *BMI* body mass index, *CVD* cardiovascular disease, *DM* diabetes mellitus, *IFG* impaired fasting glucose, *IGT* impaired glucose tolerance.

(e.g., lipopolysaccharide LPS) crossing the intestinal mucosa and entering the circulation, triggering a systemic inflammatory response, which contributes to the development of hypertension²⁸. In addition, short-chain fatty acids (SCFAs), an important product of dietary fiber fermentation by intestinal flora, have been shown to have anti-inflammatory and blood pressure regulating properties. SCFAs such as butyric acid (butyrate) and propionate can exert antihypertensive effects by binding to G protein-coupled receptors (e.g., GPR41, GPR43), promoting intestinal epithelial homeostasis, modulating immune responses, and thereby affecting vascular tone and the neuroendocrine axis²⁹. Dietary interventions have been shown to reduce inflammation levels and metabolic risk by improving intestinal flora, thereby reducing inflammation levels and metabolic risk. An umbrella review study incorporating multiple meta-analyses noted that probiotic, prebiotic, and synbiotic interventions significantly reduced insulin resistance levels (HOMA-IR) and inflammatory markers (e.g., CRP, TNF-alpha) in patients with nonalcoholic fatty liver disease (NAFLD), further supporting the potential of microecological interventions in regulating metabolism and inflammation³⁰. Whereas hypertension is closely associated with insulin resistance and chronic low-grade inflammation, this implies that improving gut microecology through diet may also have indirect but significant benefits on blood pressure control³¹. At the molecular level, intestinal flora may further participate in the regulation of glucose metabolism and energy homeostasis by regulating bile acid metabolism, increasing GLP-1 secretion, and influencing the AMPK signaling pathway, thus indirectly affecting the mechanism of hypertension²⁹. It is worth mentioning that different flora may play different or even opposite

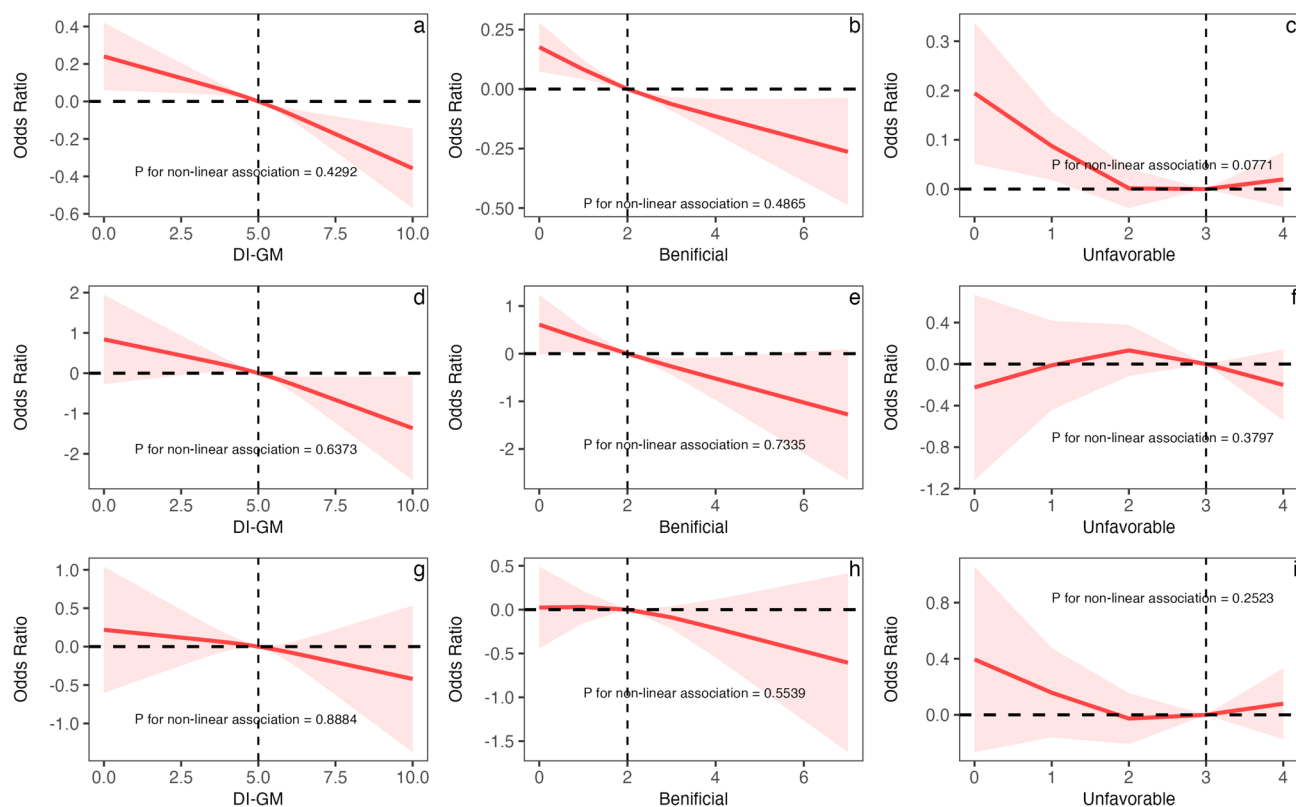


Fig. 2. Association of DI-GM with hypertension and its components systolic and diastolic blood pressure by RCS. CI, confidence interval; DI-GM, dietary index for gut microbiota; OR, odd ratio; RCS, restricted cubic spline. Panels a–c illustrate the association between DI-GM (Dietary Index for Gut Microbiota) and its components (Beneficial and Unfavorable) with hypertension. Panels d–f depict the relationship between DI-GM and its components with systolic blood pressure, while panels g–i show the relationship between DI-GM and its components with diastolic blood pressure. The trends are presented as hazard ratios modeled using restricted cubic splines (RCS). The model adjusted for age, sex, ethnicity, BMI, education level, PIR, smoking and drinking status, CVD.

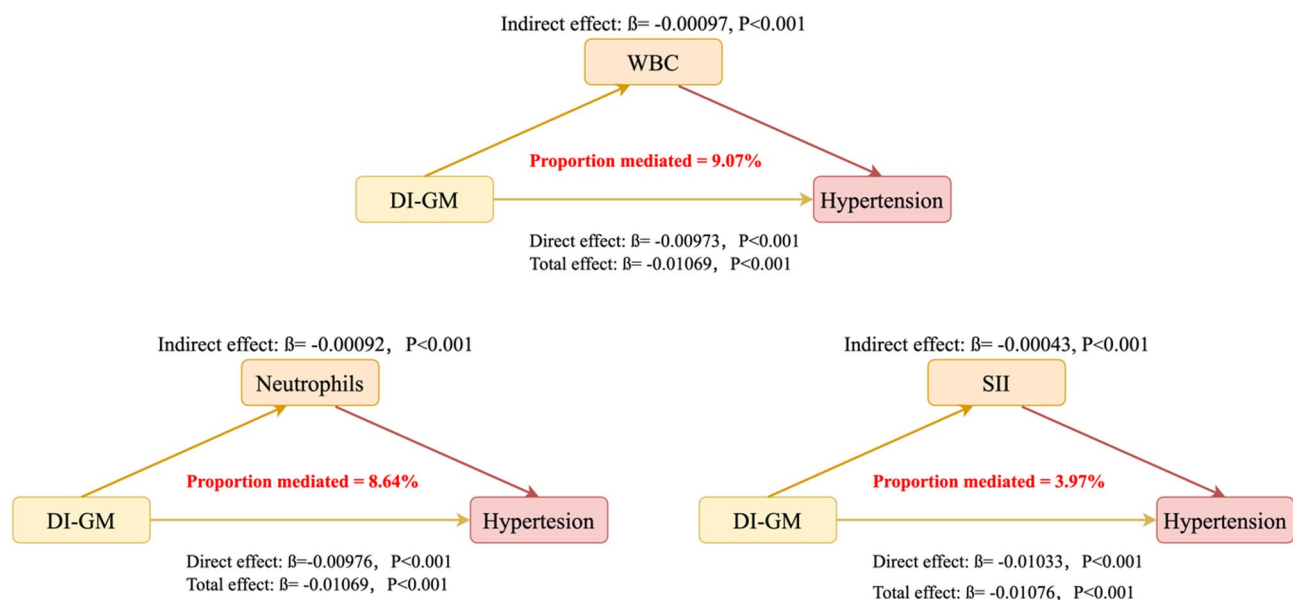


Fig. 3. Mediating role of WBC, Neutrophils and SII between DI-GM and hypertension. DI-GM, dietary index for gut microbiota. The model adjusted for age, sex, ethnicity, BMI, education level, PIR, smoking and drinking status, CVD.

roles in hypertension. For example, Akkermansia muciniphila supplementation may improve metabolic status and reduce intestinal permeability, whereas certain pathogenic genera may enhance inflammatory responses and elevate blood pressure³¹.

Notably, specific DI-GM components exhibit biologically plausible pathways linking diet to inflammation and blood pressure regulation. Green tea, containing high concentrations of epigallocatechin-3-gallate (EGCG), suppresses NF- κ B signaling through inhibition of I κ B kinase (IKK) activity, thereby reducing transcription of pro-inflammatory cytokines including IL-6 and TNF- α ³². Furthermore, beyond its direct anti-inflammatory effects, EGCG enhances gut barrier integrity by upregulating tight junction proteins (occludin, ZO-1) and promoting growth of SCFA-producing bacteria such as *Faecalibacterium prausnitzii*. A 12-week RCT demonstrated that daily green tea consumption significantly increased fecal acetate concentrations (21% increase vs. placebo) while reducing serum LPS-binding protein levels³², suggesting dual mechanisms synergistically improving metabolic homeostasis.

Conversely, regular consumption of processed meats (≥ 50 g/day) introduces heme iron and advanced glycation end products (AGEs) that promote inflammation through distinct pathways. Heme iron catalyzes ROS generation via Fenton reactions, activating the NLRP3 inflammasome in colonic macrophages and elevating IL-1 β secretion³³. Simultaneously, AGEs engage RAGE receptors to initiate MAPK/NF- κ B signaling cascades, consistent with longitudinal data showing 34% higher CRP levels in high-processed meat consumers from the ATTICA cohort³⁴. These pro-inflammatory effects are compounded by gut dysbiosis: meta-analysis evidence indicates 18% increased Proteobacteria abundance and 24% reduced Bifidobacterium following processed meat intake, accompanied by fecal calprotectin levels exceeding 50 μ g/g - a clinical marker of intestinal inflammation³³. The resultant endotoxin translocation activates systemic TLR4-mediated inflammation, creating a pathological loop that exacerbates hypertension risk.

Taken together, these mechanisms may underlie the heterogeneity observed in subgroup analyses stratified by gender, age, and ethnicity. In subgroup analyses of gender, age, and ethnicity, we further found possible heterogeneity in the effects of DI-GM. For example, female individuals may be more sensitive to DI-GM in terms of inflammation levels and gut microbial composition, which may be related to the modulatory effects of estrogen on vascular endothelial and inflammatory responses. Conversely, the antihypertensive effect of DI-GM appeared more pronounced in older adults, possibly due to their elevated baseline chronic inflammation. Notably, stronger associations were observed in younger individuals and non-Hispanic Whites. These disparities might stem from socioeconomic and cultural factors: younger populations and non-Hispanic Whites may have better access to nutrient-dense foods (e.g., higher income or education levels) or greater adherence to microbiota-friendly dietary patterns (e.g., Mediterranean diets). Prior evidence indicates that socioeconomic status strongly predicts dietary quality, with marginalized groups often facing barriers to healthy food access³⁵. Cultural preferences (e.g., higher processed meat consumption in certain ethnicities) may further modulate the DI-GM's applicability. On the other hand, no significant differences were observed in other subgroup analyses (e.g., BMI, smoking and drinking status), which may be related to the sample size or baseline characteristics of certain groups. These results suggest that differences between various subgroups need to be validated in further studies to provide tailored dietary intervention strategies for high-risk populations.

In recent years, research on diet in the management of hypertension has received considerable attention^{6,35}. The DASH diet, a dietary pattern designed to lower blood pressure, emphasizes the intake of whole grains, vegetables, and fruits while limiting saturated fat and sugar intake. Several randomized controlled trials have shown that the DASH diet is not only effective in lowering blood pressure, but also has significant cardiovascular health benefits³⁶. In addition, the Healthy Eating Index (HEI), a tool for measuring diet quality, has been shown to be strongly associated with the risk of obesity, metabolic disorders, and chronic diseases³⁷.

The results of the present study are broadly consistent with these patterns: individuals with higher DI-GM scores had a lower risk of developing hypertension, echoing the benefits observed with the DASH and Mediterranean diets. However, unlike these traditional indices that focus primarily on nutrient balance or disease risk, DI-GM is designed to reflect the microbiota-modulating potential of dietary patterns.

Our findings also align with previous studies on individual dietary components—such as sodium, fiber, and polyphenols—and their effects on gut microbiota and blood pressure regulation. High sodium intake reduces *Lactobacillus* abundance and promotes Th17-mediated inflammation. In contrast, fiber fosters the growth of SCFA-producing bacteria (*Faecalibacterium*, *Roseburia*), enhancing gut barrier function and reducing systemic inflammation. Polyphenols from green tea or berries modulate microbiota composition and inhibit pro-inflammatory pathways like NF- κ B.

By focusing on dietary components that influence microbial ecology and downstream inflammatory pathways, the DI-GM offers a complementary perspective to traditional diet indices. This mechanistic orientation enhances our understanding of how diet impacts hypertension through gut microbiota and inflammation, providing insights for future precision nutrition strategies.

While traditional dietary indices such as DASH and HEI emphasize nutrient balance or cardiovascular risk reduction, the DI-GM provides a distinct approach by focusing on dietary patterns that influence microbial composition and metabolite production. This microbiota-specific orientation offers complementary insight into diet-microbiota-inflammation-blood pressure pathways, and may inform precision nutrition strategies targeting gut health.

Despite the large-scale data analysis and important findings of this study based on the NHANES database, there are still some limitations that need to be noted. First, given the cross-sectional design, we cannot exclude the possibility of reverse causation. Individuals with existing hypertension may modify their dietary behaviors, such as reducing processed meat or increasing fiber intake, which could artificially elevate their DI-GM scores. Similarly, chronic hypertension can induce vascular endothelial dysfunction and oxidative stress, thereby amplifying systemic inflammation. Furthermore, antihypertensive treatment may potentially influence

inflammatory markers such as white blood cell (WBC) counts or neutrophil levels. To address this limitation, we conducted sensitivity analyses excluding participants using antihypertensive medications ($n = 13,679$), which yielded consistent results (Table S4). Although this approach helps reduce bias from disease management behaviors, it does not fully resolve the temporal ambiguity between diet, inflammation, and hypertension. Therefore, while our findings offer valuable insights into the diet-inflammation-blood pressure axis, they should be regarded as hypothesis-generating. Future prospective cohort studies with repeated biomarker assessments and randomized controlled trials targeting DI-GM modifications are needed to confirm these temporal relationships. We also included Fig. 3 to illustrate the hypothesized mediation pathways, which effectively functions as a conceptual directed acyclic graph (DAG). Second, the inflammatory factors (e.g., WBC and SII) used in this study may not be sufficient to comprehensively reflect the chronic inflammatory state, and more inflammatory markers (e.g., CRP, IL-6, and TNF- α) can be introduced in the future to increase the precision of measurement. In addition, the DI-GM, a scoring system based on the potential impact of diet on gut flora, does not directly measure flora diversity or abundance and does not cover nutritional factors that are classically associated with hypertension, such as sodium and potassium intake; participant dietary information may also be affected by recall bias. Third, while DI-GM has shown good correlation with gut microbiota composition in U.S. populations, its applicability in populations with distinct dietary patterns (e.g., high intake of fermented foods in East Asia or plant-based diets in South Asia) remains uncertain. Regional variations in microbiota composition and dietary habits may require adaptation of DI-GM for broader use. Future studies should validate this index in diverse cultural and geographic settings to assess its generalizability.

In summary, this study validated the significant association between DI-GM and hypertension based on a large sample of data and revealed that inflammation may play a partial mediating role. The results support the potential application of microecology-based dietary intervention strategies in the prevention and control of hypertension, and future studies should focus on mechanism validation, longitudinal design, and cross-population extrapolation to advance the deeper understanding of the “diet-gut flora-inflammation-blood pressure” pathway. The future research should focus on mechanism validation and longitudinal design and cross-population extrapolation to advance the understanding of the “diet-gut flora-inflammation-blood pressure” pathway.

Conclusion

This study identified a significant negative association between DI-GM and hypertension risk using data from NHANES 2007–2018, with stronger effects observed for systolic than diastolic blood pressure. Subgroup analyses suggested that age and ethnicity may influence this association, underscoring the importance of individualized dietary strategies.

Inflammatory factors, including white blood cell count, neutrophils, and systemic inflammatory index (SII), were found to partially mediate the relationship between DI-GM and hypertension. These findings offer insight into the mechanisms linking diet, inflammation, and blood pressure regulation.

Building on established frameworks like the DASH and Mediterranean diets, DI-GM-informed guidance may emphasize increased intake of fiber-rich plant foods, fermented products, and polyphenol-rich items to support gut health and lower hypertension risk. Future randomized controlled trials are warranted to evaluate the impact of DI-GM-based interventions—such as personalized dietary plans or microbiota-targeted education—on inflammatory markers, gut microbiota composition, and long-term blood pressure outcomes.

Data availability

The publicly available data sets used in this study can be found here: [<https://www.cdc.gov/nchs/nhanes.htm>].

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Author contributions

Jiaxin Li and Kuanlu Fan were involved in the experiment design. Jiaxin Li performed the data analysis. Jiaxin Li, Mingyue Yang, Wei Huang, Wenjing Shi, Xue Zhang, Rui Huang and Ying Zhang wrote the manuscript. Ying Zhang, Daowen Zhang, Weiwei Zhu, Cancan Liu, Nannan Xu, Huijun Zhang and Kuanlu Fan reviewed the manuscript and provided critical suggestions. Jiaxin Li, Mingyue Yang, Wei Huang, Wenjing Shi, Xue Zhang, Rui Huang and Ying Zhang revised the manuscript and improve the writing quality. Jiaxin Li and Kuanlu Fan approved the final version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

The requirement of ethical approval was waived by NCHS Research Ethics Review Board for the studies involving humans. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-19929-0>.

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