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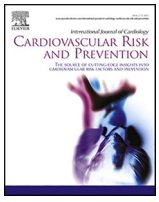

Ketogenic diets are associated with an elevated risk of hypertension: Insights from a cross-sectional analysis of the NHANES 2007–2018

Xiaolong Qu [a,1], Yuping Liu [b,1], Lei Huang [c,**], Fang Wan [a,*]

[a] Department of Cardiovascular Medicine, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
[b] Department of Nutrition, Gongli Hospital of Shanghai Pudong New Area, 219 Miao Pu Road, Shanghai, 200135, China
[c] Department of Cardiology, Renji Hospital Ningbo Branch, Shanghai Jiao Tong University School of Medicine, 1155 Binhai 2nd Road, Hangzhou Bay New District, Ningbo, 315336, China

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ABSTRACT

Background: The ketogenic diet (KD) is widely used for weight loss in obese individuals; however, its potential impact on hypertension risk remains uncertain.
Methods: We used cross-sectional data from the 2007–2018 to National Health and Nutrition Examination Survey (NHANES) to investigate the association between the dietary ketogenic ratio (DKR) and hypertension prevalence. Dietary intake information was obtained through a comprehensive 24-h dietary recall interview. The DKR values were computed using a specialized formula. Multiple logistic regression analysis was employed to examine this association, whereas nonlinear relationships were assessed using restricted cubic splines. Inflection points were determined using two-piecewise linear regression analysis. Subgroup analyses based on age were also performed.
Results: In a fully adjusted multivariate logistic regression model accounting for confounding variables, DKR was significantly associated with hypertension (OR, 1.24; 95 % CI: 1.00–1.53; P = 0.045). Moreover, individuals in the highest quartile of DKR exhibited a significantly elevated risk of hypertension compared with those in the lowest quartile (OR, 1.15; 95 % CI: 1.07–1.24; P < 0.001). Additionally, restricted cubic spline analysis revealed a linear relationship between DKR and the risk of hypertension, with a turning point identified at 3.4 units on the measurement scale employed for this study's purposes. Subgroup analyses indicated that this association between DKR and hypertension was particularly pronounced among individuals aged ≥40 years, especially those age group–40-60. We further observed that a multivariate linear regression analysis revealed a significant positive correlation between DKR and DBP in a fully adjusted model (β, 0.42; 95 % CI: 0.12–0.87; P = 0.018), indicating that as DKR increased, there was an accompanying increase in DBP. However, no significant correlation was found between SBP and DKR (β, 0.11; 95 % CI: −0.37-0.59; P = 0.655).
Conclusion: The KD may enhance susceptibility to hypertension in middle-aged and elderly populations in the United States, exhibiting a strong association with elevated diastolic blood pressure, while no significant correlation was observed with increased systolic blood pressure.

1. Introduction

The ketogenic diet (KD) is a high-fat, low-carbohydrate diet that has gained popularity in recent years for its purported health benefits, including weight loss and improved metabolic health [1]. However, there is growing concern about the potential negative effects of the KD on certain health outcomes, such as cardiovascular health. One such concern is the possible link between KD and increased risk of hypertension.

Hypertension, or high blood pressure, is a major risk factor for cardiovascular disease, stroke, and other serious health conditions [2]. It is estimated that nearly half of adults in the United States have hypertension, making it a significant public health concern [3]. Given the increasing popularity of KD and the prevalence of hypertension in the population, it is important to investigate the potential relationship between the two.

* Corresponding author. 160 Pujian Road, Pudong New Area, Shanghai, 200135, China.
** Corresponding author. 1155 Binhai 2nd Road, Hangzhou Bay New District, Ningbo, 315336, China.
E-mail addresses: huanglei6854@outlook.com (L. Huang), gshlsh20012005@126.com (F. Wan).
[1] These authors share the first authorship on this work.

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Previous studies have reported conflicting findings on the association between KD and hypertension. Some studies have suggested that KD may have a protective effect on blood pressure, possibly due to weight loss and improved insulin sensitivity [4]. However, other studies have found that the KD may actually increase the risk of hypertension, possibly due to the high fat and sodium content of the diet [5].

In light of these conflicting findings, further research is required to clarify the relationship between KD and hypertension. This observational study aimed to investigate the association between adherence to KD and the risk of hypertension using data from the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2018. By analyzing a large, nationally representative sample of adults, we hope to provide valuable insights into the potential impact of KD on blood pressure regulation.

2. Materials and methods

2.1. Data source and study population

This study used data from the 2007–2018 to NHANES, which is publicly accessible through the NHANES database (https://www.cdc.gov/nchs/nhanes). Fig. 1 illustrates the screening process for the study population. A total of 59,842 participants were included in this study. However, individuals under the age of 20 (N = 25,072), those with missing dietary data (N = 3,984), those with missing hypertension data (N = 40), and those with missing covariate data (N = 406) were excluded from the analysis. Ultimately, the complete information of 30,340 adults was included in the final analysis. All participants provided written informed consent and the trial protocol was approved by the ethics review board of the National Center for Health Statistics. Informed consent was obtained from all NHANES participants.

2.2. Definition of hypertension

Participants were considered to have hypertension if they met the following criteria: (1) received a diagnosis of hypertension (also called high blood pressure) from a physician or other healthcare professional; (2) self-reported use of antihypertensive medications (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, diuretics, and/or fixed-dose combinations); and (3) had high blood pressure measurements (systolic ≥140 mmHg or diastolic ≥90 mmHg). The NHANES database included three consecutive blood pressure measurements and additional measurements when necessary.

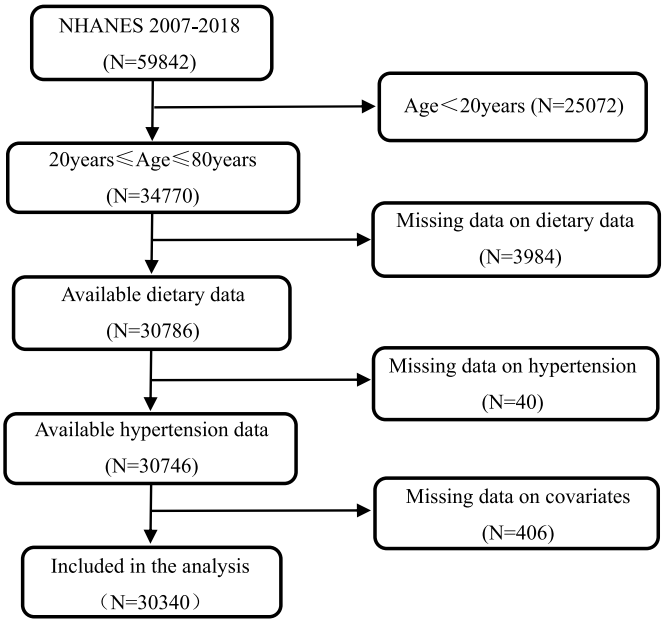

Fig. 1. Flow diagram of the study participant selection. NHANES, National Health and Nutrition Examination Survey.

2.3. Dietary intake data

Dietary intake data were collected through two 24-h retrospective NHANES interviews conducted by a professional dietary interviewer. The initial interview was carried out in person, followed by a second telephone interview 3–10 days later. During the follow-up interview, participants were asked to recall and report the type and quantity of food and beverages consumed in the preceding 24 h, with dietary intake estimated based on the average of the two 24-h recall data [6]. Energy and nutrient intakes for all foods were calculated using the Food and Nutrient database from the Diet Study [7].

2.4. The dietary ketogenic ratio (DKR)

To evaluate the predictive dietary patterns for achieving nutritional ketosis, we calculated the DKR based on the proportion of macronutrients that have ketogenic and antiketogenic properties. The DKR of macronutrients was determined using the equation developed by Withrow [8]. In brief, it was calculated as (0.9×grams fat + 0.46×grams protein) divided by (0.1×grams fat + 0.58 ×grams protein + grams net carbohydrate), resulting in a range from zero to nine. Higher DKR values indicated diets with a greater likelihood of inducing nutritional ketosis.

2.5. Covariates

Information regarding sociodemographic and lifestyle characteristics was obtained from the demographic and questionnaire data. This included information on age (Youth group,≤40 years old; Middle-aged group, 40–60 years old and Elderly group,≥60 years old), gender, race/ethnicity (Mexican American, Non-Hispanic White, Non-Hispanic Black, Other Hispanic, Other Race), educational level (Less than High school, High school/GED, More than high school), family income to poverty ratio (PIR), marital status (Married, Widowed, Divorced, Separated, Never married, Living with partner), smoking status, Body Mass Index (BMI,kg/cm2) (< 18.5 kg/m2,18.5–24 kg/m2.24–28 kg/m2, ≥28kg/m2), systolic blood pressure (SBP); diastolic blood pressure (DBP); and physical activity (inactive, active, mildly active, and highly active). Participants were categorized as smokers if they responded affirmatively to the question “Have you smoked at least 100 cigarettes in your entire life?” Conversely, those who answered negatively were classified as nonsmokers. Standing height (cm) and weight (kg) were measured at the mobile examination center. The BMI was calculated by dividing the weight by the square of the standing height.

Physical activity levels were assessed based on participants’ self-reported frequency and duration of various physical activities during a typical week. Participants provided information on the number of days and duration they engaged in high- and moderate-intensity activities, such as walking or cycling, as well as high- and moderate-intensity sports, fitness, or recreational activities at work. The duration of each activity, the number of days per week it was performed, and the metabolic equivalent (MET) score recommended by NHANES (vigorous work-related activity: 8.0; Moderate work-related activity: 4.0; Walking or cycling for transport: 4.0; Leisure-related vigorous activity: 8.0; Leisure-related moderate activity: 4.0) were assessed in MET-minutes per week. Met/week was calculated by multiplying the total number of minutes per week for each activity by the Met value recommended by the NHANES [9]. Finally, the sum of all activities for each participant was calculated and participants were classified as “inactive” (0-MET minutes per week), “lightly active” (0 to <500 MET-minutes per week), “active” (500 to <1000 MET-minutes per week), or “highly active” (1000 MET-minutes per week) [10].

Participants were considered to have a history of cardiovascular disease if they had been diagnosed with congestive heart failure or coronary heart disease by a medical professional. The presence of stroke, chronic kidney disease (CKD), and cancer was determined through questionnaire responses. Diabetes was defined as HbA1c $\geq$ 6.5 % or the self-reported use of glucose-lowering medications.

Multiple imputation techniques were employed to handle missing values for covariates with a proportion of missingness below 10 %. However, participants with missing values equal to or exceeding 10 %, such as smoking status and CKD, were also subjected to imputation but were retained in the subsequent analysis.

3. Statistical analysis

The participants were stratified into two groups based on the presence of hypertension. Descriptive analyses were conducted to summarize baseline characteristics, with continuous variables presented as mean ± standard deviation (SD) or median (interquartile range), and categorical variables were reported as counts (percentages). Between-group comparisons were performed using appropriate statistical tests: Student's t-test for normally distributed continuous variables, Wilcoxon rank-sum test for non-normally distributed variables, and chi-square test for categorical variables. Multiple logistic regression models were used to investigate the association between the DKR and hypertension risk. Quartiles of DKR were used to calculate the odds ratios (ORs), with Q1 serving as the reference group in Model A, which included unadjusted covariates. Model B was adjusted for age, educational level, race, marital status, and PIR. In Model C, additional covariates included BMI, Physical activity, diabetes mellitus, coronary heart disease, heart failure, stroke history, and cancer diagnosis.

To examine the dose-response relationship between DKR and the prevalence of hypertension, we employed multivariable adjusted restricted cubic splines (RCS) in model C to explore potential nonlinear associations.

Statistical significance was determined using a two-tailed p-value of less than 0.05. All data were analyzed using the SPSS 27 software. The data were generated using GraphPad Prism 9.4 and R version 3.6.

4. Results

4.1. Participants characteristics

The baseline characteristics of the study participants are presented in Table 1. Participants with hypertension exhibited significant differences compared to those without hypertension in terms of age, race, education level, marital status, PIR, BMI, physical activity status, smoking status, and the presence of diseases (diabetes, coronary heart disease, congestive heart failure, chronic kidney disease, stroke, and cancer). Specifically, individuals with hypertension were characterized by advanced age and marital status as well as a higher prevalence of smoking habits and lower levels of education and PIR. Moreover, they demonstrated reduced physical activity levels but higher BMIs along with an increased incidence of other diseases.

The baseline nutrient intake characteristics of the participants are presented in Table 2. Significant differences were observed in the consumption of total energy, carbohydrates, fats,proteins, sugar, dietary fiber, vitamins, and trace elements between the two groups. Specifically, the hypertension group exhibited a lower intake of energy, carbohydrates, fats, proteins, sugar, dietary fiber, and other nutrients compared to the non-hypertension group. Additionally, a higher DKR value was observed in the hypertensive group than in the non-hypertensive group.

4.2. The correlation between DKR and hypertension

Three models were constructed to investigate the association between DKR and hypertension (Table 3). Model A revealed a significant

Table 1
Baseline characteristics of participants by hypertension, National Health and Nutrition Examination Survey 2007–2018.

Characteristic	Hypertension		p-value
	Yes, N = 11,030	No, N = 19,310	
Gender (%)			0.162
Male	5,299 (48.0 %)	9,438 (48.9 %)	
Female	5,731 (52.0 %)	9,872 (51.1 %)	
Age (%)			<0.001
Youth group	1,388 (12.6 %)	9,333 (48.3 %)	
Middle-aged group	3,772 (34.2 %)	6,378 (33.0 %)	
Elderly group	5,870 (53.2 %)	3,599 (18.6 %)	
Race/ethnicity (%)			<0.001
Mexican American	1,247 (11.3 %)	3,284 (17.0 %)	
Other Hispanic	1,038 (9.4 %)	2,113 (10.9 %)	
Non-Hispanic White	4,737 (42.9 %)	7,887 (40.8 %)	
Non-Hispanic Black	3,043 (27.6 %)	3,522 (18.2 %)	
Other Race	965 (8.7 %)	2,504 (13.0 %)	
Education Level (%)			<0.001
Less than High school	2,960 (26.8 %)	4,338 (22.5 %)	
High school/GED	2,705 (24.5 %)	4,258 (22.1 %)	
More than high school	5,355 (48.6 %)	10,714 (55.5 %)	
Marital Status (%)			<0.001
Married	5,779 (52.4 %)	9,717 (50.3 %)	
Widowed	1,524 (13.8 %)	811 (4.2 %)	
Divorced	1,521 (13.8 %)	1,813 (9.4 %)	
Separated	413 (3.7 %)	628 (3.3 %)	
Never married	1,171 (10.6 %)	4,449 (23.0 %)	
Living with partner	622 (5.6 %)	1,892 (9.8 %)	
PIR (%)			<0.001
≤1.5	3,952 (35.8 %)	6,747 (34.9 %)	
1.5–2.5	2,460 (22.3 %)	4,057 (21.0 %)	
> 2.5	4,618 (41.9 %)	8,506 (44.0 %)	
BMI (%)			<0.001
< 18.5 kg/m^2	86 (0.8 %)	384 (2.0 %)	
18.5–24 kg/m^2	1,334 (12.1 %)	4,910 (25.4 %)	
24–28 kg/m^2	2,494 (22.6 %)	5,509 (28.5 %)	
≥ 28 kg/m^2	7,116 (64.5 %)	8,507 (44.1 %)	
SBP(mmHg)			<0.001
Median (IQR)	132 (120, 144)	116 (108, 126)	
DBP(mmHg)			<0.001
Median (IQR)	72 (64, 80)	68 (62, 76)	
Physical activity (%)			<0.001
Inactive	3,863 (35.0 %)	4,239 (22.0 %)	
Active	1,118 (10.1 %)	1,917 (9.9 %)	
Mildly active	1,517 (13.8 %)	2,257 (11.7 %)	
Highly active	4,532 (41.1 %)	10,897 (56.4 %)	
Smoke (%)			<0.001
Yes	5,416 (49.1 %)	7,666 (39.7 %)	
No	5,614 (50.9 %)	1,164 (60.3 %)	
Diabetes (%)			<0.001
Yes	2,815 (25.5 %)	1,176 (6.1 %)	
No	7,781 (70.5 %)	17,863 (92.5 %)	
Borderline	434 (3.9 %)	271 (1.4 %)	
Coronary heart disease (%)			<0.001
Yes	946 (8.6 %)	283 (1.5 %)	
No	10,084 (91.4 %)	19,027 (98.5 %)	
Heart failure (%)			<0.001
Yes	790 (7.2 %)	171 (0.9 %)	
No	10,240 (92.8 %)	19,139 (99.1 %)	
Stroke (%)			<0.001
Yes	898 (8.1 %)	267 (1.4 %)	
No	10,132 (91.9 %)	19,043 (98.6 %)	
CKD (%)			<0.001
Yes	1,876 (17.0 %)	2,695 (14.0 %)	
No	9,154 (83.0 %)	16,615 (86.0 %)	
Cancer (%)			<0.001
Yes	1,719 (15.6 %)	1,233 (6.4 %)	
No	9,311 (84.4 %)	18,077 (93.6 %)	

Abbreviations:PIR, Ratio of family income to poverty; BMI, Body Mass Index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CKD, Chronic Kidney Disease.

Table 2
Intakes of energy and nutrients baseline characteristics.

Characteristic	Hypertension		p-value
	Yes, N = 11,030	No, N = 19,310	
Energy (kcal)			<0.001
Median (IQR)	1,802 (1,324, 2,417)	1,996 (1,482, 2,668)	
Protein (gm)			<0.001
Median (IQR)	69 (49, 95)	76 (54, 103)	
Carbohydrate (gm)			<0.001
Median (IQR)	216 (156, 292)	242 (174, 324)	
Total fat (gm)			<0.001
Median (IQR)	67 (44, 97)	73 (49, 105)	
Total sugars (gm)			<0.001
Median (IQR)	87 (54, 133)	99 (62, 148)	
Dietary fiber (gm)			<0.001
Median (IQR)	14 (9, 21)	15 (10, 22)	
Folate (mcg)			<0.001
Median (IQR)	322 (215, 468)	352 (236, 507)	
Vitamin A (mcg)			0.075
Median (IQR)	460 (253, 759)	468 (253, 778)	
Vitamin C (mcg)			<0.001
Median (IQR)	51 (21, 109)	53 (21, 118)	
Vitamin E (mg)			<0.001
Median (IQR)	6.4 (4.0, 9.8)	6.8 (4.4, 10.5)	
Magnesium (mg)			<0.001
Median (IQR)	254 (184, 347)	275 (199, 372)	
Zinc (mg)			<0.001
Median (IQR)	9 (6, 13)	10 (7, 14)	
Selenium (mcg)			<0.001
Median (IQR)	95 (65, 134)	103 (71, 145)	
DKR (%)			<0.001
Q1	2,424 (22.0 %)	4,524 (23.4 %)	
Q3	2,771 (25.1 %)	4,770 (24.7 %)	
Q2	2,725 (24.7 %)	4,942 (25.6 %)	
Q4	3,110 (28.2 %)	5,074 (26.3 %)	

Abbreviations:DKR, Dietary ketogenic ratio.

OR of 1.6 (95 % CI: 1.34–1.91; P < 0.001), indicating a positive correlation between each unit increase in DKR and an elevated risk of hypertension. Model B also demonstrated a significant OR of 1.63 (95 % CI: 1.33–2.00; P < 0.001), further supporting the observed association, whereas model C showed a slightly attenuated but still statistically significant OR of 1.24 (95 % CI: 1.00–1.53; P = 0.045).

4.3. Stratification analysis based on age

Subgroup analyses stratified by age groups revealed a significant positive association between an increased DKR and the risk of hypertension among middle-aged (40–60 years) and elderly (>60 years) participants, even after adjusting for confounding variables in model C. Notably, this association was more pronounced in the middle-aged group (OR [95%CI]: 1.90 [1.41,2.55]; P < 0.001). However, no significant association was observed between DKR and hypertension in young adults (≤40 years), even after controlling for potential confounders. In both the middle-aged and elderly groups, higher DKR levels were positively correlated with a greater prevalence of hypertension; specifically, the odds ratios for Q4 group were 1.28 (1.14,1.43) and 1.11 (1.02,1.25), respectively, as shown in Table 4.

4.4. DKR and hypertension risk based on RCS

The analysis, employing RCS adjusted for model C, revealed a significant linear association between DKR and the risk of hypertension (P = 0.491 for non-linear trend), demonstrating an overall J-shaped relationship, as illustrated in Fig. 2. Two-stage linear regression was used to further investigate the threshold effect of DKR on hypertension. In Table 6, the inflection point is determined to be at 3.4 units. Beyond this threshold, each incremental increase in DKR showed a statistically insignificant but 3 % increase in the risk of developing hypertension.

4.5. The correlation between DKR and SBP and DBP

Furthermore, our multivariate linear regression analysis revealed a significant positive correlation between DKR and SBP prior to adjusting for confounding factors (β,0.76; 95 % CI:0.20–1.31; P = 0.007); however, this correlation was not significant in models B (β,0.36; 95 % CI: -0.12–0.84; P = 0.145) and C (β,0.11; 95 % CI: -0.37–0.59; P = 0.655) after accounting for confounders. Conversely, across all three models with both unadjusted (β,0.83; 95 % CI:0.44–1.22; P < 0.001) and fully adjusted confounding factors (β,0.42; 95 % CI:0.12–0.87; P = 0.018), DKR exhibited a significantly positive association with DBP. These findings suggest that the relationship between DKR and DBP is stronger compared to that with SBP, indicating an amplified increase in DBP as DKR rises (Table .5).

5. Discussion

The results of this study demonstrate a positive association between KD adherence and the risk of hypertension. Specifically, a higher proportion of individuals adhering to the KD exhibited an increased susceptibility to developing hypertension, particularly among those aged 40 years and above, with a more pronounced impact observed within the 40–60 age group. We further observed that a multivariate linear regression analysis revealed a significant positive correlation between DKR and DBP in a fully adjusted model, indicating that as DKR increased, there was an accompanying increase in DBP. However, no significant correlation was found between SBP and DKR. In conclusion, these findings suggest that strict adherence to the KD may potentially elevate the risk of developing hypertension, particularly through an elevation in diastolic blood pressure. The observed association between the KD and hypertension risk in our analysis of NHANES data necessitates a more comprehensive investigation into the underlying mechanisms that potentially contribute to this relationship.

The metabolic shift from carbohydrate to fat metabolism in the KD leads to the production of ketone bodies, which may impact blood

Table 3
OR and 95 % CI for Hypertension according to according to quartiles of DKR.

Characteristic	Model A			Model B			Model C		
	OR	95 % CI	p-value	OR	95 % CI	p-value	OR	95 % CI	p-value
Q1	Ref.		–	Ref.		–	Ref.		–
Q2	1.03	1.01, 1.10	0.008	1.05	0.97, 1.13	0.244	1.10	1.02, 1.19	0.012
Q3	1.08	1.01, 1.16	0.020	1.11	1.03, 1.20	0.009	1.05	1.01, 1.13	0.042
Q4	1.14	1.07, 1.22	<0.001	1.16	1.07, 1.25	<0.001	1.15	1.07, 1.24	<0.001
DKR	1.6	1.34,1.91	<0.001	1.63	1.33,2.00	<0.001	1.24	1.00,1.53	0.045

Abbreviations: CI, confidence interval; OR, odds ratio; DKR, Dietary ketogenic ratio.
Model A:unadjusted covariates.
Model B:adjusted by age, education level, race, marital status, and PIR.
Model C:adjusted by age, education level, race, marital status, PIR,BMI, physical activity, diabetes mellitus, coronary heart disease, heart failure, stroke history, and cancer.

Table 4
OR and 95 % CI for hypertension according to quartiles of DKR base on age groups.

Characteristic	Youth group			Middle-aged group			Elderly group		
	OR	95 % CI	p-value	OR	95 % CI	p-value	OR	95 % CI	p-value
Q1	Ref.		–	Ref.		–	Ref.		–
Q2	1.06	0.90, 1.25	0.471	1.15	1.02, 1.29	0.021	1.09	0.97, 1.23	0.153
Q3	1.05	0.89, 1.23	0.575	1.10	1.01, 1.14	0.017	1.07	0.95, 1.20	0.273
Q4	1.05	0.89, 1.23	0.578	1.28	1.14, 1.43	<0.001	1.11	1.02, 1.25	0.048
DKR	1.43	0.93,2.17	0.075	1.90	1.41,2.55	<0.001	1.61	1.16,2.25	0.005

Abbreviations: CI, confidence interval; OR, odds ratio; DKR, Dietary ketogenic ratio.
Model C:adjusted by age, education level, race, marital status, PIR,BMI, physical activity, diabetes mellitus, coronary heart disease, heart failure, stroke history, and cancer.

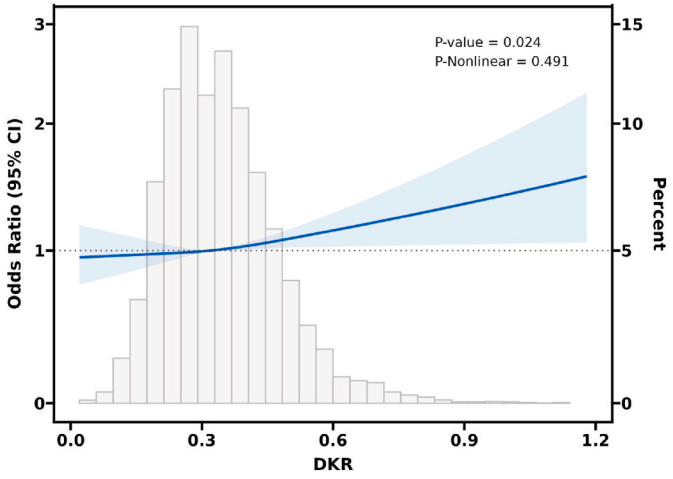

Fig. 2. Association between DKR levels and the risks of hypertension with restricted cubic splines (RCS). DKR, Dietary ketogenic ratio; Cl, confidence interval; OR, odds ratio.

Table 5
OR and 95 % CI for SBP and DBP according to the DKR.

Characteristic	β	95 % CI	p-value
SBP			
Model A	0.76	0.20, 1.31	0.007
Model B	0.36	−0.12, 0.84	0.145
Model C	0.11	−0.37, 0.59	0.655
DBP			
Model A	0.83	0.44, 1.22	<0.001
Model B	0.45	0.06, 0.84	0.023
Model C	0.42	0.12, 0.87	0.018

Abbreviations: CI, confidence interval; OR, odds ratio; DKR, Dietary ketogenic ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure.
Model A:unadjusted covariates.
Model B:adjusted by age, education level, race, marital status, and PIR.
Model C:adjusted by age, education level, race, marital status, PIR,BMI, physical activity, diabetes mellitus, coronary heart disease, heart failure, stroke history, and cancer.

pressure through various mechanisms. While ketones have been shown to enhance mitochondrial efficiency and reduce oxidative stress in certain tissues [11], their overall effect on blood pressure regulation is complex and may involve changes in vascular tone and cardiac function [12]. Dietary patterns high in fat, such as those observed in the KD, can influence electrolyte balance and intravascular volume status. Sodium retention and alterations in potassium homeostasis could potentially contribute to elevated blood pressure levels [13]. Recent research has emphasized the significance of maintaining electrolyte balance for hypertension development, particularly within dietary patterns that promote high-fat intake [14]. Chronic inflammation and oxidative stress

Table 6
Effect of DKR on hypertension: adjusted odds ratios from segmented logistic regression analysis.

Characteristic	OR	95 % CI	p-value
DKR (< 0.34)	0.83	0.38, 1.83	0.64
DKR (≥0.34)	1.40	1.04, 2.16	0.02

Abbreviations: CI, confidence interval; OR, odds ratio; DKR, Dietary ketogenic ratio.
Two-piecewise logistic-regression model was used to calculate the threshold effect of the DKR.
Model was adjusted for age, education level, race, marital status, PIR,BMI, Physical activity, diabetes mellitus, coronary heart disease, heart failure, stroke history, and cancer.

have been implicated in the pathogenesis of hypertension. The impact of the KD on inflammatory markers and oxidative stress levels may be a critical factor in regulating blood pressure [15]. However, some studies suggest that the KD may induce a low-grade inflammatory state and oxidative stress, potentially exacerbating endothelial dysfunction and vascular remodeling [16]. Endothelial dysfunction is a key factor in hypertension development. The effects of the KD on endothelial function may be multifaceted, with evidence suggesting that ketone bodies can impair endothelial nitric oxide synthase activity, thereby reducing vasodilation and contributing to elevated blood pressure [17].

Insulin resistance is closely associated with hypertension and cardiovascular risk. Although the KD may enhance insulin sensitivity in the short term, its long-term effects on insulin resistance and blood pressure remain uncertain. Recent research suggests that the KD may have varying impacts on insulin resistance, which could potentially affect blood pressure regulation [18]. The sustained adherence to the KD may have implications for cardiovascular health beyond its immediate benefits for weight loss and glycemic control. Studies indicate that the KD's influence on lipid profiles and endothelial function might have adverse consequences for cardiovascular risk [19,20].

Our findings reveal a stronger correlation between DKR and hypertension in individuals aged 40 years or older, possibly reflecting age-related changes in cardiovascular function. Age-related declines in renal function and vascular elasticity could interact with the metabolic effects of the KD to influence blood pressure levels [21].

6. Limitations

To ensure a comprehensive understanding of the research findings, it is crucial to emphasize the limitations of this study. Firstly, despite employing rigorous data processing and statistical analysis techniques that revealed potential trends suggesting an association between a ketogenic diet and hypertension, there are significant constraints in investigating the relationship due to the absence of direct measurement methods for ketosis levels. This hypothetical inference may not accurately reflect the true state of ketosis and could potentially impact our research results. Therefore, future studies will employ more precise

methodologies to directly measure ketosis levels in order to fully evaluate its potential association with hypertension.

Additionally, this study solely relied on self-reported questionnaires for assessing dietary habits without conducting repeated measurements, which may introduce temporal instability when estimating dietary patterns. Although NHANES database provides appropriate design features and reliable data selection along with rigorous statistical analysis methods that offer valuable insights into exposure factors associated with health or disease status, it cannot establish direct causal relationships.

To overcome this limitation, future studies need to explicitly discuss using more stringent methods such as multiple repeat questionnaires or other objective tools for evaluating dietary habits to ensure accurate and consistent assessment of dietary patterns. Through further scientific exploration and technological innovation efforts, we aim at gaining a more comprehensive understanding of both benefits and potential harms brought by a ketogenic diet while making significant contributions towards public health initiatives.

7. Conclusion

The observed association between the KD and hypertension, as indicated by our analysis, necessitates further investigation into the long-term health implications of this dietary approach. Elucidating the underlying mechanisms through which the KD may impact cardiovascular well-being is imperative for formulating evidence-based dietary recommendations.

CRediT authorship contribution statement

Xiaolong Qu: Writing – original draft, Validation, Resources, Methodology, Investigation, Data curation. **Yuping Liu:** Data curation, Formal analysis, Investigation, Writing – original draft. **Lei Huang:** Writing – review & editing, Visualization, Supervision, Project administration, Methodology. **Fang Wan:** Project administration, Supervision, Visualization, Writing – review & editing.

Data availability

The data can be accessed publicly through the National Center for Health Statistics website on https://www.cdc.gov/nchs/nhanes.

Declaration of competing interest

The authors assert that they do not possess any known conflicting financial interests or personal relationships that could potentially exert influence on the findings presented in this paper.

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