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Social determinants of health and mortality on hyperuricemia adults in the USA from 2007 to 2016: a national cohort study

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Abstract

Background Hyperuricemia is associated with higher all-cause and cardiovascular mortality. However, the role of social determinants of health (SDoH) in this context remains unclear. This study aims to examine the relationship between SDoH, hyperuricemia, all-cause and cardiovascular mortality, and explore the mediating role of SDoH in these relationships.

Methods This cohort study analyzed data from 23,919 US adults (aged ≥ 20) in the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2016, with linked mortality data through December 31, 2019. Two primary exposures were examined: hyperuricemia, defined as serum uric acid level > 420 μmol/L in males and > 360 μmol/L in females, and SDoH, which encompassed education level, marital status, income-to-poverty ratio (PIR), food security, health insurance, regular health-care access, housing instability, and employment. The primary outcomes were all-cause and cardiovascular mortality. Statistical methods included logistic regression, Cox proportional hazard model, and mediation analysis.

Results The study cohort had a mean (SD) age of 49.27 (17.63) years, with 48.28% (95%CI, 47.69%-48.86%) being male, and 68.52% (95%CI, 65.27%-71.60%) identified as non-Hispanic White. Having three or more unfavorable SDoH significantly mediated the link between hyperuricemia and both all-cause and cardiovascular mortality. SDoH ≥ 6, SDoH = 5, SDoH = 4, and SDoH = 3 mediated 20.30% ($P = 0.004$), 13.94% ($P = 0.044$), 23.59% ($P = 0.018$), and 13.88% ($P = 0.008$) of the association between hyperuricemia and all-cause mortality, respectively. SDoH ≥ 6, SDoH = 5, SDoH = 4, and SDoH = 3 mediated 15.35% ($P = 0.006$), 14.87% ($P = 0.050$), 20.68% ($P = 0.026$), and 9.45% ($P = 0.012$) of the association between hyperuricemia and cardiovascular mortality.

Conclusions SDoH significantly mediated the relationship between hyperuricemia and both all-cause and cardiovascular mortality.

Keywords SDoH, Hyperuricemia, All-cause mortality, Cardiovascular mortality, NHANES

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Introduction

Hyperuricemia, characterized by elevated uric acid levels in the blood, can result from either excessive production or reduced excretion of uric acid, the end product of purine metabolism. The deposition of urate crystals in joints and other tissues can trigger an inflammatory response, leading to gouty arthritis [1]. This condition currently affects an estimated 8.3 million Americans [2], with its prevalence steadily increasing from 19.1% during 1988–1994 to 21.5% in 2007–2008 [3]. As a globally prevalent metabolic disorder, hyperuricemia is strongly associated with increased all-cause and cardiovascular mortality [4, 5]. Despite significant advances in understanding the biological mechanisms underlying the association between hyperuricemia and adverse health outcomes [6–11], the role of non-biological factors, particularly social factors, remains poorly understood. Increasing evidence suggests that social determinants of health (SDoH) play a critical role in mortality disparities [12–15], highlighting the substantial impact of the social environment on health status and disease progression.

The US Healthy People 2030 framework delineates the five key domains of SDoH: economic stability, education quality and opportunities, healthcare access and quality, community and built environments, and social and community contexts [16]. Although SDoH are acknowledged as significant determinants of the onset and progression of certain diseases [17, 18], their impact on the relationship between hyperuricemia and mortality remains understudied. This study aims to fill this knowledge gap by examining the interplay between biological and social factors and exploring the potential mediating effect of SDoH on the relationship between hyperuricemia and all-cause and cardiovascular mortality. The findings of this study will provide novel insights into the role of non-biological factors in the development of hyperuricemia while offering valuable scientific evidence to inform public health policy and reduce health disparities.

Materials and methods

Study population

This cohort study utilized data from the National Health and Nutrition Examination Survey (NHANES), a comprehensive survey designed to collect health information from the US population [19]. NHANES employs a stratified multistage random sampling methodology to ensure a nationally representative sample [20]. The survey protocol was approved by the National Center for Health Statistics review board, and all participants provided informed consent through signed agreements. The data for this study were sourced from the NHANES database. Due to the lack of key variables in data from other years, the study ultimately included data from 2007 to 2016, comprising a total of 50,588 participants. To ensure the integrity and reliability of the study's findings, we applied specific exclusion criteria. We excluded individuals under the age of 20 ($N = 21{,}387$), those with missing essential data ($N = 5{,}252$), including exposure factors, mediating variables, and covariates, as well as those with incomplete mortality data ($N = 50$). After applying these exclusions, the final study population comprised 23,919 participants (Fig. 1). Due to the representativeness of the NHANES database and the application of weighting methods in the study, it was reasonable to conclude that the remaining study population reliably represented the overall sample, ensuring the scientific validity and credibility of the results.

Hyperuricemia and social determinants of health

In this study, based on previous research on hyperuricemia, hyperuricemia was defined as serum uric acid level > 420 μmol/L in males and > 360 μmol/L in females [21–23]. This study integrated definitions of SDoH from previous research [12, 24–26] and aligned them with the standards outlined in the Healthy People 2030 initiative in the United States. Eight specific items related to the subdomains of SDoH were included in the study: education level, marital status, income-to-poverty ratio (PIR), food security, health insurance, regular healthcare access, housing instability, and employment status [16]. The detailed definitions of the SDoH domains and their sub-items are provided in Supplementary Table 1. To evaluate the cumulative impact of SDoH, we summed the eight dichotomized SDoH variables, assigning a value of 0 for each favorable level and 1 for each unfavorable level. Since only a small proportion of participants reported six, seven, or eight unfavorable SDoH, these categories were combined, resulting in a cumulative SDoH variable ranging from 0 to 6 or more. The sample sizes for the SDoH categories are as follows: 2,684 for SDoH = 0; 3,484 for SDoH = 1; 3,742 for SDoH = 2; 3,805 for SDoH = 3; 3,838 for SDoH = 4; 3,394 for SDoH = 5; and 2,972 for SDoH ≥ 6. The sample size within each SDoH category was substantial enough to perform the analysis effectively. Additionally, when analyzing the disparities of SDoH across different populations, SDoH was categorized into three levels: low burden (SDoH = 0–2), moderate burden (SDoH = 3–5), and high burden (SDoH = 6–8).

All-cause and cardiovascular mortality

Mortality data for this study were obtained from the NHANES public-use linked mortality file, updated through December 31, 2019, in conjunction with the National Death Index (NDI) provided by the National Center for Health Statistics (NCHS). The follow-up period began from the date of survey participation and

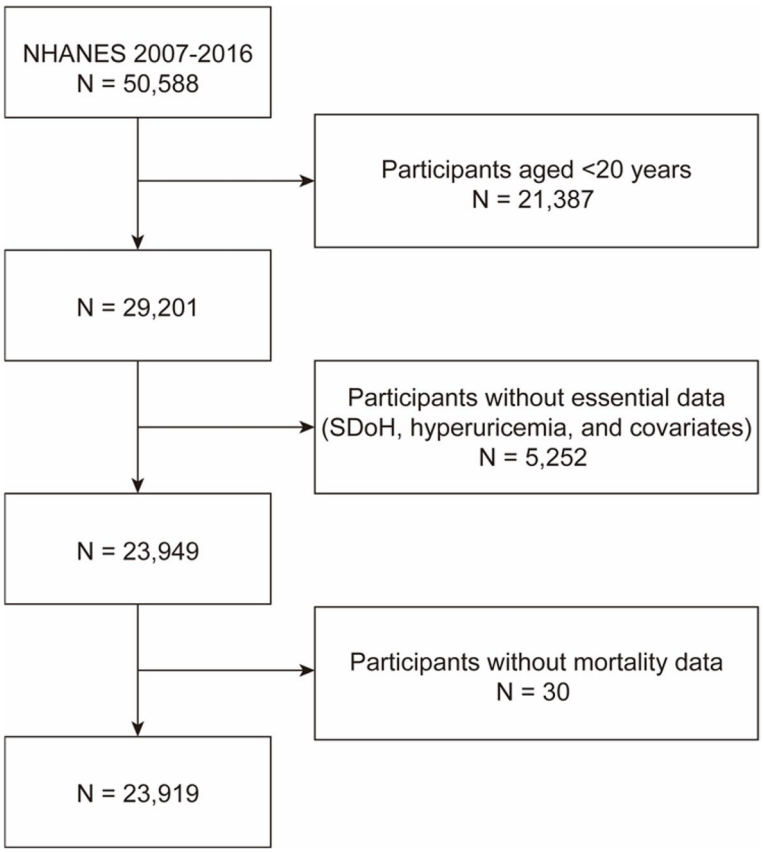

Fig. 1 Flowchart of study participants

continued until December 31, 2019. Causes of death were identified using the International Statistical Classification of Diseases, 10 th Revision (ICD-10). Cardiovascular mortality was categorized based on deaths from heart diseases (I00-I09, I11, I13, I20-I51) and cerebrovascular diseases (I60-I69) [27].

Covariates

The covariates considered in this study included age, sex, race/ethnicity, body mass index (BMI), drinking and smoking status, diabetes, gout, cardiovascular diseases (CVD) and cancer or malignancy. Race/ethnicity was categorized into five groups: Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other races. Smoking status was classified based on whether the individual had ever smoked 100 or more cigarettes in their lifetime, or fewer than 100 cigarettes. Drinking status was categorized as having consumed 12 or more alcoholic drinks in the past 12 months, or fewer than 12 drinks. BMI was calculated as weight (in kilograms) divided by the square of height (in meters) and grouped into three categories (< 25, 25–29.9, ≥ 30 kg/m^2). CVD, and cancer/malignancy diagnoses were based on self-reported physician diagnoses obtained during personal interviews, using standardized medical condition questionnaires. CVD included heart failure, coronary artery disease, angina, myocardial infarction, and stroke.

Statistical analysis

Data analysis was performed following the Centers for Disease Control and Prevention (CDC) guidelines, utilizing NHANES sample weights (WTMEC2YR) to ensure a representative sample of the US population. Baseline characteristics were categorized based on the presence of hyperuricemia. Continuous variables were compared using survey-weighted linear regression, and survey-weighted Pearson $\chi 2$ tests were employed for categorical variables. Continuous data was presented as means with 95% confidence intervals (CIs), and categorical data as weighted percentages. The relationship between hyperuricemia and both all-cause and cardiovascular mortality was examined using multivariate Cox proportional hazard model, with results expressed as hazard ratios (HRs) and 95%CI, and all models passed the Schoenfeld residuals test. Model 1 was unadjusted, while Model 2 was

adjusted for gender, age, and race. Model 3 was further adjusted for BMI, drinking and smoking status, diabetes, gout, CVD, and cancer or malignancy. Kaplan–Meier survival curves were generated, and between-group differences were assessed using the log-rank test. Additionally, multivariate logistic regression was used to analyze the relationship between SDoH and hyperuricemia, while Cox proportional hazards model was applied to explore the associations between SDoH and mortality, as well as between hyperuricemia and mortality. Mediation analysis was performed to assess the potential mediating role of SDoH, adjusting for the same covariates. All statistical analyses were conducted using R software (version 4.4.1) and STATA (version 16.0). Two-tailed P values <0.05 were considered indicative of statistical significance. Data analysis was performed from September 10 to November 15, 2024.

Results

Baseline characteristics

Among the 23,919 US adults, the mean (SD) age was 49.27 (17.63) years, with males accounting for 48.28% (95% CI, 47.69%–48.86%) of the population and 68.52% (95% CI, 65.27%–71.60%) identifying as non-Hispanic White. Individuals with hyperuricemia had a significantly higher mean age than those without hyperuricemia. Furthermore, the hyperuricemia group exhibited a higher proportion of males compared to females. Within the hyperuricemia group, non-Hispanic Whites comprised the largest proportion, followed by non-Hispanic Blacks (Table 1). Significant differences were observed in the distribution of gender, age, race, and BMI across different SDoH groups ($P< 0.001$) (Fig. 2).

Association of hyperuricemia with all-cause and cardiovascular mortality

The mean follow-up duration in this study was 91.86 months, ranging from 1 to 160 months, with an interquartile range (IQR) of 62 to 123 months. A total of 2,570 deaths from all causes and 782 cardiovascular-related deaths were documented. Table 2 illustrates the association between hyperuricemia and both all-cause and cardiovascular mortality. After adjusting for all covariates in Model 3, a significant positive association was observed between hyperuricemia and all-cause mortality (HR, 1.40; 95% CI, 1.25–1.57) as well as cardiovascular mortality (HR, 1.65; 95% CI, 1.36–2.02). The Kaplan–Meier survival curves in Fig. 3 further reinforce this finding, demonstrating significantly lower survival rates for individuals with hyperuricemia compared to those without hyperuricemia, for both all-cause mortality ($P< 0.001$) and cardiovascular mortality ($P< 0.001$).

Association of SDoH with hyperuricemia and mortality

Table 3 illustrates the association between hyperuricemia and SDoH. After adjusting for all covariates, Model 3 revealed a positive association between hyperuricemia and SDoH $=3$ (OR, 1.28; 95% CI, 1.10–1.50), SDoH $=4$ (OR, 1.24; 95% CI, 1.05–1.46), and SDoH ≥ 6 (OR, 1.27; 95% CI, 1.02–1.58). Table 4 demonstrates the relationship between SDoH and mortality outcomes. After adjusting for all covariates, Model 3 indicated a positive association between increasing SDoH levels and all-cause mortality, with the risk progressively rising as SDoH values accumulated. Similarly, except for the SDoH $=1$ group, other SDoH levels showed a positive association with cardiovascular mortality, with the risk escalating as SDoH values accumulated.

Mediating role of SDoH indicators

The mediation analysis revealed that the presence of three or more SDoH significantly mediated the relationship between hyperuricemia and both all-cause and cardiovascular mortality. Figures 4 and 5 illustrate the potential mediating effects of SDoH on the associations between hyperuricemia and mortality outcomes. All the analysis results were presented in Supplementary Table 2. The results showed that various SDoH levels mediated significant percentages of these associations. For all-cause mortality, SDoH ≥ 6 mediated 20.30% of the association ($P=0.004$), while SDoH $=5$, SDoH $=4$, and SDoH $=3$ mediated 13.94% ($P= 0.044$), 23.59% ($P= 0.018$), and 13.88% ($P= 0.008$) of the association, respectively. Similarly, for cardiovascular mortality, SDoH ≥ 6 mediated 15.35% of the association ($P= 0.006$), while SDoH $=5$, SDoH $=4$, and SDoH $=3$ mediated 14.87% ($P= 0.050$), 20.68% ($P= 0.026$), and 9.45% ($P= 0.012$) of the association, respectively. Although the mediation effects for SDoH $=1$ and SDoH $=2$ did not reach statistical significance, it was noteworthy that the effect for SDoH $=2$ approached significance for both mortality outcomes ($P= 0.058$). Additionally, the negative mediation effects observed for SDoH $=1$ across both mortality outcomes suggested a potential threshold effect in the mediation pathway.

Discussion

This cohort study, based on a nationally representative sample of 23,919 U.S. adults, is the first study to explore the association between SDoH, hyperuricemia, all-cause mortality, and cardiovascular mortality. Notably, our analysis elucidated the mediating role of SDoH in these associations, yielding insights into how SDoH may influence health outcomes related to hyperuricemia. The fully adjusted model revealed that individuals

Table 1 Baseline characteristics of participants according to hyperuricemia, NHANES 2007–2016

Characteristics	Hyperuricemia exposure			*P* value
	All (*n* = 23,919)	No (*n* = 19,495)	Yes (*n* = 4424)	
Age, y	47.24 (46.74–47.75)	46.45 (45.92–46.98)	50.95 (50.26–51.64)	< 0.001
Gender				
Male	48.28 (47.69–48.86)	46.69 (45.93–47.44)	55.72 (53.99–57.43)	< 0.001
Female	51.72 (51.14–52.31)	53.31 (52.56–54.07)	44.28 (42.57–46.01)	
Race				
Mexican American	8.23 (6.71–10.05)	8.71 (7.11–10.63)	5.95 (4.67–7.56)	< 0.001
Other Hispanic	5.40 (4.39–6.62)	5.74 (4.68–7.03)	3.79 (2.94–4.86)	
Non-Hispanic White	68.52 (65.27–71.60)	67.92 (64.61–71.05)	71.31 (67.92–74.48)	
Non-Hispanic Black	10.47 (9.01–12.13)	10.10 (8.70–11.69)	12.21 (10.28–14.44)	
Other Race	7.39 (6.54–8.34)	7.53 (6.65–8.51)	6.75 (5.73–7.93)	
Education level				
High school graduate or higher	83.72 (82.27–85.07)	83.69 (82.18–85.10)	83.82 (82.13–85.37)	0.853
Less than high school	16.28 (14.93–17.73)	16.31 (14.90–17.82)	16.18 (14.63–17.87)	
Marital status				
Married or living with a partner	63.67 (62.25–65.06)	64.16 (62.73–65.58)	61.33 (59.05–63.57)	0.005
Not married nor living with a partner	36.33 (34.94–37.75)	35.84 (34.42–37.27)	38.67 (36.43–40.95)	
PIR				
≥ 300%	48.96 (46.71–51.22)	49.53 (47.24–51.83)	46.29 (43.34–49.26)	0.006
< 300%	51.04 (48.78–53.29)	50.47 (48.17–52.76)	53.71 (50.74–56.66)	
Food security				
Full food security	76.33 (74.84–77.76)	76.32 (74.77–77.80)	76.40 (74.46–78.24)	0.914
Marginal, low, or very low	23.67 (22.24–25.16)	23.68 (22.20–25.23)	23.60 (21.76–25.54)	
Health insurance				
Private insurance	63.10 (61.31–64.86)	63.38 (61.48–65.23)	61.83 (59.34–64.26)	0.194
Government or no insurance	36.90 (35.14–38.69)	36.62 (34.77–38.52)	38.17 (35.74–40.66)	
Regular health-care access				
At least one regular healthcare facility	85.21 (84.36–86.02)	84.84 (83.96–85.67)	86.94 (85.46–88.28)	0.004
None or emergency room	14.79 (13.98–15.64)	15.16 (14.33–16.04)	13.06 (11.72–14.54)	
Housing instability				
Own home	67.30 (65.39–69.17)	66.86 (64.80–68.86)	69.38 (67.09–71.59)	0.025
Rent or other arrangement	32.70 (30.83–34.61)	33.14 (31.14–35.20)	30.62 (28.41–32.91)	
Employment status				
Employed, student, or retired	63.66 (62.32–64.99)	64.74 (63.32–66.12)	58.65 (56.39–60.87)	< 0.001
Unemployed	36.34 (35.01–37.68)	35.26 (33.88–36.68)	41.35 (39.13–43.61)	
Cumulative number of unfavorable SDoH				
0	18.32 (17.03–19.69)	18.54 (17.13–20.04)	17.29 (15.61–19.12)	0.004
1	19.21 (18.15–20.32)	19.69 (18.60–20.82)	16.99 (14.99–19.19)	
2	17.17 (16.38–17.99)	16.94 (16.06–17.85)	18.26 (16.60–20.06)	
3	14.56 (13.94–15.21)	14.21 (13.57–14.88)	16.21 (14.86–17.67)	
4	12.83 (12.10–13.59)	12.73 (12.00–13.49)	13.31 (12.03–14.70)	
5	10.04 (9.33–10.80)	10.11 (9.38–10.88)	9.75 (8.64–10.99)	
≥ 6	7.86 (7.16–8.61)	7.79 (7.06–8.59)	8.18 (7.25–9.22)	
All-cause mortality				
No	92.17 (91.58–92.71)	93.33 (92.82–93.80)	86.75 (85.21–88.15)	< 0.001
Yes	7.83 (7.29–8.42)	6.67 (6.20–7.18)	13.25 (11.85–14.79)	
Cardiovascular mortality				
No	97.74 (97.47–97.98)	98.23 (98.02–98.42)	95.44 (94.53–96.21)	< 0.001
Yes	2.26 (2.02–2.53)	1.77 (1.58–1.98)	4.56 (3.79–5.47)	

Table 1 (continued)

Characteristics	Hyperuricemia exposure			*P* value
	All (*n* = 23,919)	No (*n* = 19,495)	Yes (*n* = 4424)	
Smoking status				
≥ 100 cigarettes/life	44.65 (43.34–45.97)	43.87 (42.41–45.35)	48.30 (46.45–50.16)	< 0.001
< 100 cigarettes/life	55.35 (54.03–56.66)	56.13 (54.65–57.59)	51.70 (49.84–53.55)	
Drinking status				
≥ 12 drinks/year	71.88 (70.47–73.24)	71.82 (70.36–73.24)	72.13 (70.05–74.12)	0.747
< 12 drinks/year	28.12 (26.76–29.53)	28.18 (26.76–29.64)	27.87 (25.88–29.95)	

Percentages are weighted. Differences in baseline characteristics were assessed using survey-weighted linear regression for continuous variables and survey-weighted Pearson χ2 tests for categorical variables

Abbreviations: *PIR* poverty-to-income ratio, *SDoH* social determinants of health, *BMI* body mass index, *CVD* Cardiovascular diseases

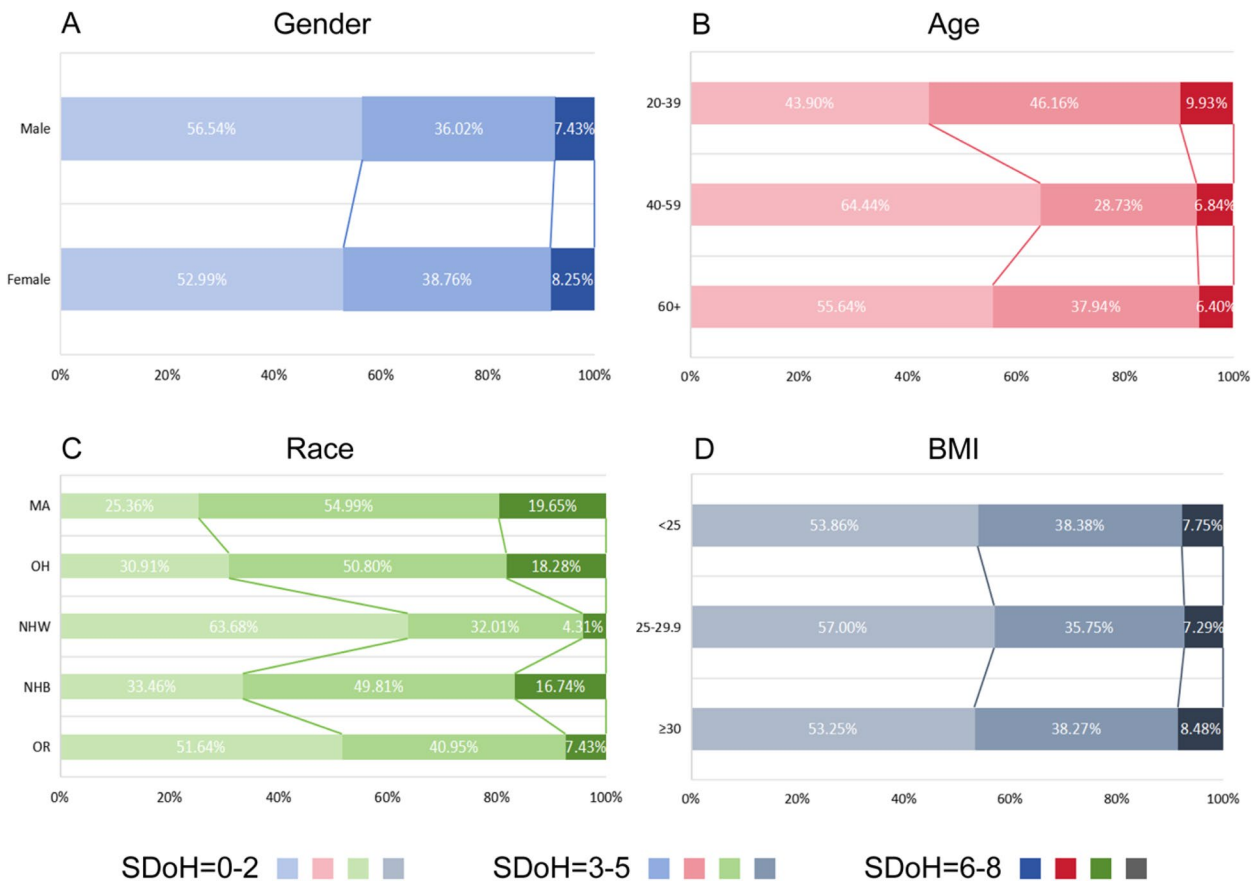

Fig. 2 Characteristics of the SDoH across different population groups. **A** Characteristics of the SDoH across different genders. **B** Characteristics of the SDoH across different age groups. **C** Characteristics of the SDoH across different races. **D** Characteristics of the SDoH across different BMI categories. Percentages are weighted. Differences in baseline characteristics were assessed using survey-weighted Pearson χ2 tests for categorical variables. Abbreviations: MA, Mexican American; OH, Other Hispanic; NHW, Non-Hispanic White; NHB, Non-Hispanic Black; OR, Other Race; BMI, body mass index

with hyperuricemia had significantly higher risks of all-cause and cardiovascular mortality compared to their counterparts without hyperuricemia. The results demonstrated a significant positive association between SDoH, hyperuricemia, and mortality outcomes. Furthermore, mediation analysis showed that the presence of three or more adverse SDoH factors significantly mediated the relationship between hyperuricemia and both all-cause

Table 2 Association of hyperuricemia with all-cause mortality and cardiovascular mortality

	Model 1		Model 2		Model 3	
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**	**HR (95% CI)**	***P* value**
All-cause mortality						
Hyperuricemia	2.04 (1.85–2.25)	< 0.001	1.46 (1.30–1.64)	< 0.001	1.40 (1.25–1.57)	< 0.001
Cardiovascular mortality						
Hyperuricemia	2.65 (2.22–3.17)	< 0.001	1.81 (1.50–2.18)	< 0.001	1.65 (1.36–2.02)	< 0.001

Model 1: unadjusted for any covariate

Model 2: adjusted for age, gender, and race

Model 3: adjusted for age, gender, race, BMI, drinking and smoking status, diabetes, gout, CVD, and cancer or malignancy

The results in the table were based on multivariate Cox proportional hazard model

Abbreviations: *SDoH* social determinants of health, *BMI* body mass index, *CVD* cardiovascular diseases, *HR* hazard ratio, *CI* confidence interval

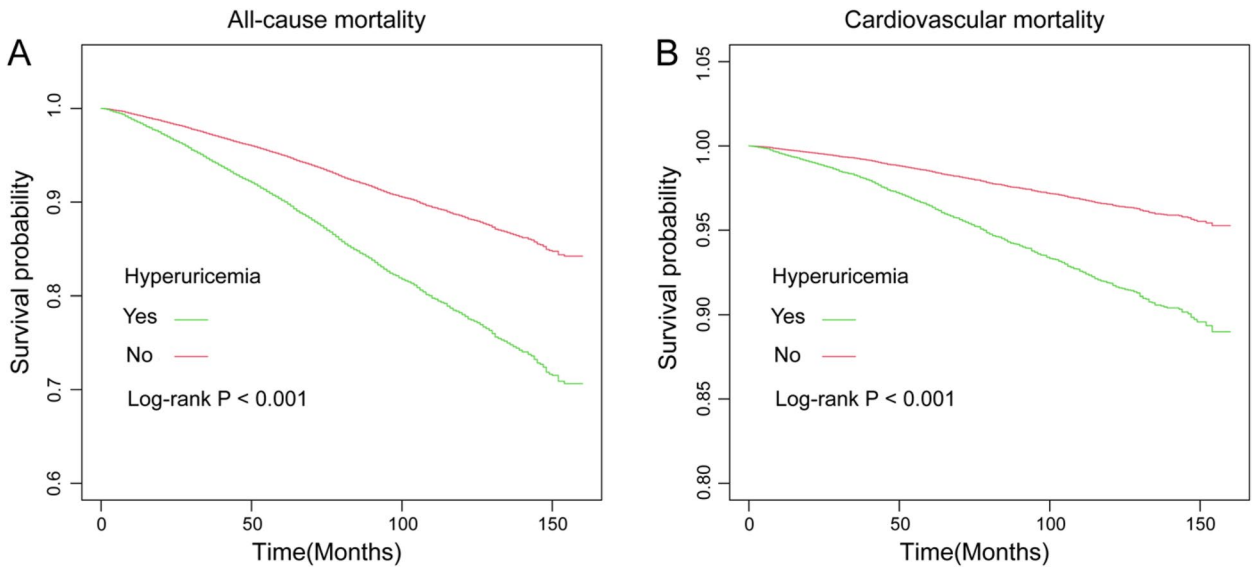

Fig. 3 Kaplan–Meier survival curves for participants with and without hyperuricemia. **A** All-cause mortality; **B** Cardiovascular mortality

Table 3 The association between hyperuricemia and SDoH

	Model 1		Model 2		Model 3	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Hyperuricemia						
Cumulative number of unfavorable SDoH						
0	Reference		Reference		Reference	
1	0.93 (0.78–1.09)	0.363	0.92 (0.77–1.08)	0.308	0.91 (0.77–1.07)	0.260
2	1.16 (0.98–1.37)	0.096	1.16 (0.98–1.38)	0.092	1.14 (0.96–1.35)	0.155
3	1.22 (1.05–1.42)	0.010	1.29 (1.11–1.51)	0.002	1.28 (1.10–1.50)	0.003
4	1.12 (0.97–1.30)	0.134	1.25 (1.06–1.46)	0.008	1.24 (1.05–1.46)	0.014
5	1.04 (0.89–1.21)	0.661	1.19 (1.02–1.40)	0.033	1.19 (1.00–1.41)	0.057
≥ 6	1.13 (0.93–1.36)	0.220	1.28 (1.03–1.60)	0.031	1.27 (1.02–1.58)	0.036

Model 1: unadjusted for any covariate

Model 2: adjusted for age, gender, and race

Model 3: adjusted for age, gender, race, BMI, drinking and smoking status, diabetes, gout, CVD, and cancer or malignancy

The results in the table were based on multivariate logistic regression

Abbreviations: *BMI* body mass index, *CVD* cardiovascular diseases, *OR* odds ratio, *CI* confidence interval

Table 4 The association of SDoH with all-cause mortality and cardiovascular mortality

	Model 1		Model 2		Model 3	
	HR (95%CI)	***P* value**	**HR (95%CI)**	***P* value**	**HR (95%CI)**	***P* value**
All-cause mortality						
Cumulative number of unfavorable SDoH						
0	Reference		Reference		Reference	
1	3.52 (2.38–5.21)	< 0.001	2.37 (1.60–3.52)	< 0.001	2.19 (1.47–3.25)	< 0.001
2	5.82 (3.96–8.54)	< 0.001	3.28 (2.23–4.83)	< 0.001	2.89 (1.97–4.24)	< 0.001
3	7.56 (5.23–10.92)	< 0.001	4.85 (3.33–7.09)	< 0.001	4.27 (2.93–6.21)	< 0.001
4	7.05 (4.82–10.33)	< 0.001	5.78 (3.93–8.49)	< 0.001	4.76 (3.24–7.00)	< 0.001
5	7.19 (5.01–10.31)	< 0.001	7.45 (5.09–10.91)	< 0.001	6.00 (4.10–8.79)	< 0.001
≥ 6	7.09 (4.96–10.13)	< 0.001	8.38 (5.83–12.05)	< 0.001	6.52 (4.54–9.37)	< 0.001
Cardiovascular mortality						
Cumulative number of unfavorable SDoH						
0	Reference		Reference		Reference	
1	3.43 (1.64–7.17)	0.001	1.87 (0.91–3.86)	0.090	1.79 (0.85–3.74)	0.124
2	8.00 (3.82–16.76)	< 0.001	3.36 (1.61–7.01)	0.001	3.08 (1.47–6.46)	0.003
3	11.10 (5.43–22.69)	< 0.001	5.22 (2.59–10.54)	< 0.001	4.67 (2.31–9.45)	< 0.001
4	9.52 (4.61–19.67)	< 0.001	5.85 (2.87–11.96)	< 0.001	4.94 (2.38–10.23)	< 0.001
5	9.39 (4.60–19.17)	< 0.001	7.64 (3.79–15.37)	< 0.001	6.16 (3.01–12.58)	< 0.001
≥ 6	10.08 (4.97–20.45)	< 0.001	9.71 (4.84–19.50)	< 0.001	7.62 (3.74–15.51)	< 0.001

Model 1: unadjusted for any covariate

Model 2: adjusted for age, gender, and race

Model 3: adjusted for age, gender, race, BMI, drinking and smoking status, diabetes, gout, CVD, and cancer or malignancy

The results in the table were based on multivariate Cox proportional hazard model

Abbreviations: *SDoH* social determinants of health, *BMI* body mass index, *CVD* cardiovascular diseases, *HR* hazard ratio, *CI* confidence interval

and cardiovascular mortality. These findings suggest that SDoH may be a key underlying mechanism driving these associations, highlighting the significant role of social factors in shaping health outcomes. This study provides valuable evidence for mitigating hyperuricemia-related risks, emphasizing the importance of addressing social determinants to improve health outcomes.

The concept of SDoH has a long history dating back to the early twentieth century [28]. However, it gained significant attention with the 2008 World Health Organization (WHO) report establishing SDoH as a central framework for understanding the impact of socioeconomic factors on health. In recent years, a growing body of research has explored the associations between SDoH and adverse clinical outcomes, including cardiovascular diseases [29], Alzheimer's disease [30], asthma [31], cancer [32], and premature death [12]. These studies have consistently demonstrated the critical role that socioeconomic factors play in the onset and progression of diseases. This study classified SDoH into three categories: low burden (SDoH = 0–2), moderate burden (SDoH = 3–5), and high burden (SDoH = 6–8). This classification enabled an examination of the distribution of SDoH across different groups. The distribution of SDoH burdens varied significantly across some demographic groups. Individuals aged 20–39 were disproportionately represented in the moderate and high SDoH burden categories. This is likely due to factors such as employment instability, economic pressure, and family building, which are commonly experienced during this life stage. Non-Hispanic White individuals were underrepresented in the moderate and high SDoH burden categories compared to other racial groups. This difference may reflect existing disparities in social resources, educational opportunities, and health insurance coverage. In contrast, the differences in SDoH distribution across different genders and BMI levels show relatively minimal variation.

Hyperuricemia, a common metabolic disorder, is a well-established independent risk factor for cardiovascular diseases [33], kidney diseases [34], and metabolic syndrome [35]. The results of this study corroborate and extend this evidence, demonstrating that individuals with hyperuricemia had significantly higher all-cause and cardiovascular mortality rates compared to their counterparts without hyperuricemia, even after adjusting for potential confounding factors. The Kaplan–Meier survival curves provided further support for this association, revealing significantly lower survival rates for

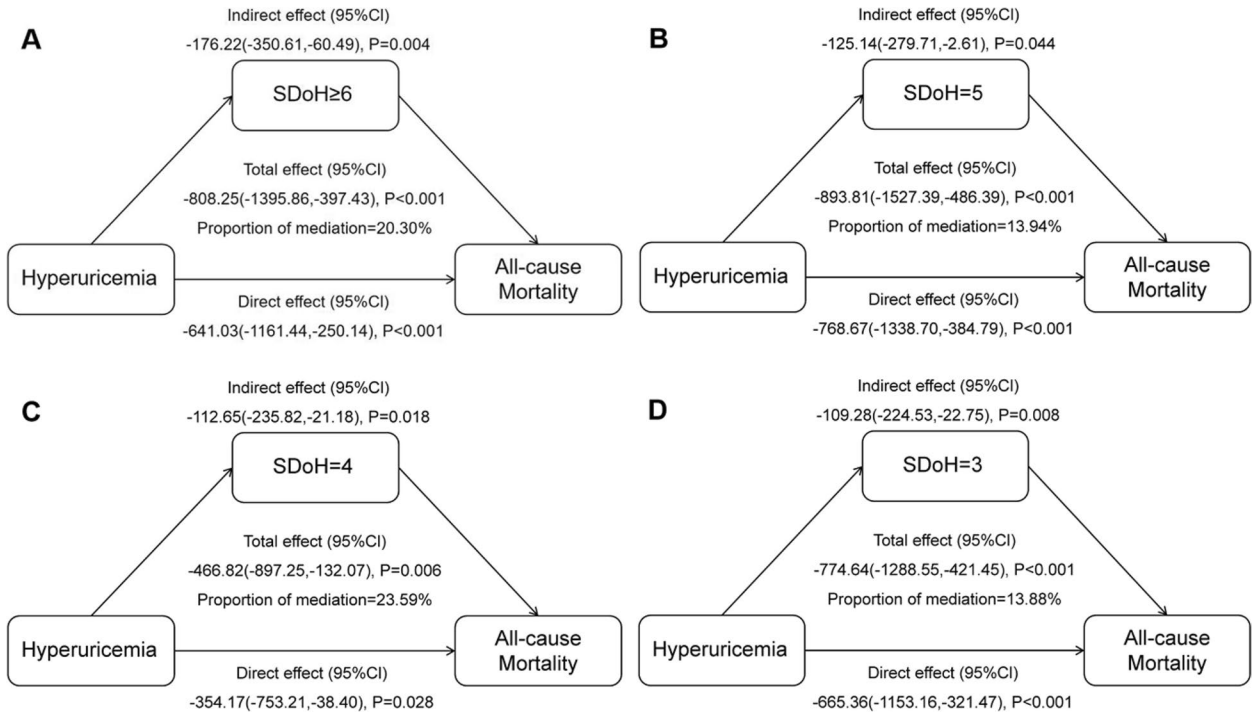

Fig. 4 Mediating role of SDoH in the association between hyperuricemia and all-cause mortality. **A** Mediating role of SDoH ≥ 6 in the association between hyperuricemia and all-cause mortality. **B** Mediating role of SDoH = 5 in the association between hyperuricemia and all-cause mortality. **C** Mediating role of SDoH = 4 in the association between hyperuricemia and all-cause mortality. **D** Mediating role of SDoH = 3 in the association between hyperuricemia and all-cause mortality. Analysis adjusted for age, gender, race, BMI, drinking and smoking status, diabetes, gout, CVD, and cancer or malignancy

all-cause and cardiovascular mortality among individuals with hyperuricemia. Previous meta-analyses have consistently demonstrated a significant association between hyperuricemia and increased risks of all-cause and cardiovascular mortality. For instance, a meta-analysis of 11 studies involving 172,123 participants found that hyperuricemia increased the risk of all-cause mortality [36]. Another meta-analysis of 9 studies involving 25,229 participants also revealed a strong association between hyperuricemia and both all-cause and cardiovascular mortality [37]. While numerous studies have investigated the biological factors and mechanisms associated with hyperuricemia, the socioeconomic factors contributing to this condition have received relatively little attention. This knowledge gap motivated the present study, which aimed to explore the relationships between SDoH, hyperuricemia, all-cause mortality, and cardiovascular mortality, with a particular focus on the potential mediating role of SDoH in these relationships. The results indicated a significant positive association between higher SDoH scores and hyperuricemia. Mediation analysis revealed a potential mediating role of SDoH in the relationship between hyperuricemia and mortality rates. Notably, having three or more adverse SDoH factors was found to be a critical threshold, significantly mediating the relationship between hyperuricemia and both all-cause and cardiovascular mortality. Taking SDoH ≥ 6 as an example, it accounted for 15.35% of the mediating effect of hyperuricemia on all-cause mortality, indicating that 15.35% of the total effect of hyperuricemia on all-cause mortality was realized through this pathway. This finding emphasized the need for clinicians to consider social determinants of health when assessing mortality risk in patients with hyperuricemia, as these factors could affect health outcomes. In policy development, it was crucial to recognize the impact of social determinants and improve socioeconomic conditions and education levels to lower mortality risk in these patients.

SDoH act as sources of chronic social, psychological, and environmental stress, triggering a cascade of physiological responses that ultimately exacerbate disease outcomes. Specifically, SDoH stimulate the sympathetic nervous-adrenal medullary axis and the hypothalamic–pituitary–adrenal axis, leading to elevated levels of stress hormones, including cortisol and catecholamines [38]. These hormonal changes induce inflammatory responses, promoting adverse disease outcomes. Prolonged exposure to unfavorable

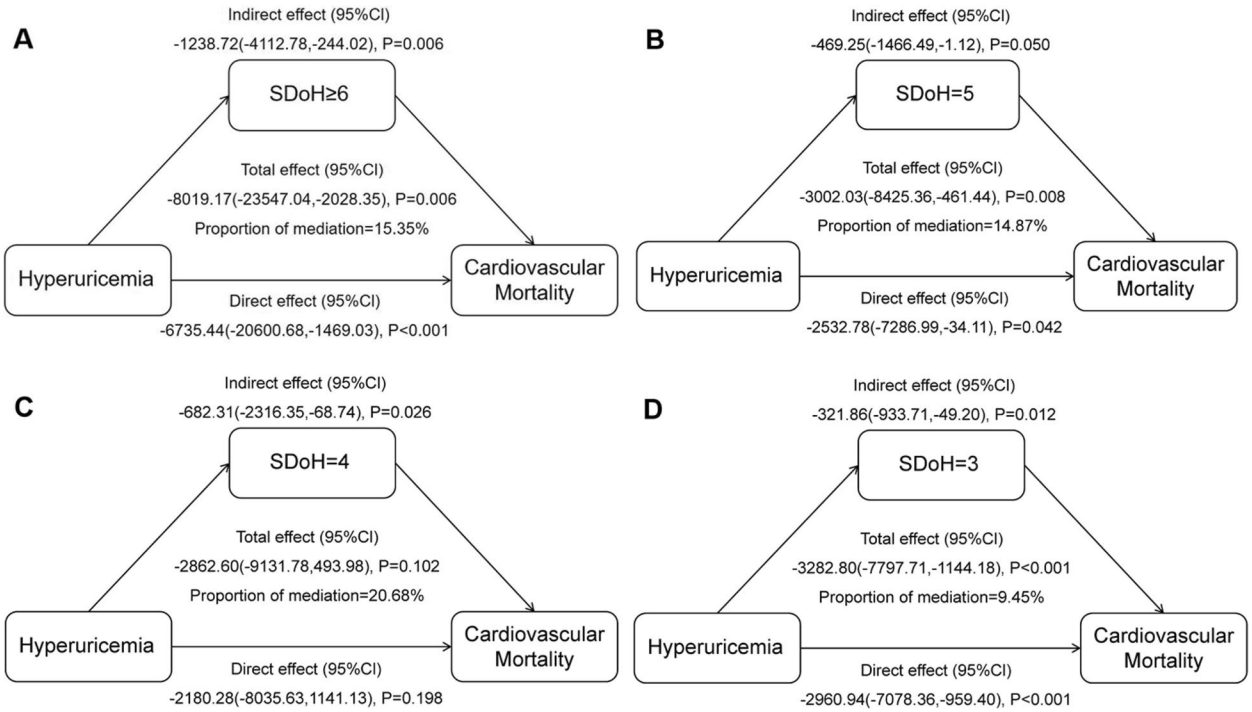

Fig. 5 Mediating role of SDoH in the association between hyperuricemia and cardiovascular mortality. **A** Mediating role of SDoH ≥ 6 in the association between hyperuricemia and cardiovascular mortality. **B** Mediating role of SDoH = 5 in the association between hyperuricemia and cardiovascular mortality. **C** Mediating role of SDoH = 4 in the association between hyperuricemia and cardiovascular mortality. **D** Mediating role of SDoH = 3 in the association between hyperuricemia and cardiovascular mortality. Analysis adjusted for age, gender, race, BMI, drinking and smoking status, diabetes, gout, CVD, and cancer or malignancy

SDoH further compromises the body's anti-inflammatory response by inducing glucocorticoid receptor resistance [39], thereby perpetuating chronic inflammation. Chronic activation of these pathways also disrupts β2-adrenergic receptor signaling, activating pro-inflammatory pathways and further aggravating inflammation [40]. Moreover, unfavorable SDoH were shown to be associated with increased levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), which further intensifies the inflammatory burden [41]. Inflammation could elevate uric acid levels through multiple mechanisms. In a chronic inflammatory state, pro-inflammatory factors such as IL-6 and TNF-α may downregulate the expression or function of renal uric acid transporters, including ABCG2 and URAT1, thereby reducing uric acid excretion [42]. Additionally, inflammation accelerated cellular damage and purine metabolism, leading to the release of large amounts of ATP and other substrates, which were converted into uric acid through the xanthine oxidase (XO) pathway. Inflammatory factors such as IL-1β could directly enhance XO activity, further increasing uric acid production [43, 44]. SDoH have been shown to influence the immune system by affecting the proliferation and clonal hematopoiesis in the bone marrow and spleen, thereby impacting the function and distribution of immune cells [45]. For example, chronic stress was found to increase activity in the amygdala, activating the neuro-hematopoietic-inflammatory axis, which is believed to contribute to the progression of CVD [46]. SDoH also impact disease outcomes through gene-environment interactions and intergenerational transmission [47]. Prolonged exposure to psychosocial and environmental stress has been shown to accelerate cellular aging, primarily by inducing inflammation and oxidative stress [48]. Previous studies have demonstrated the association between low socioeconomic status and epigenetic aging, characterized by DNA methylation [49] and telomere shortening [50]. Individuals residing in disadvantaged communities often exhibit more pronounced changes in gene expression [49]. Moreover, the biological effects of SDoH are transmitted across generations, affecting the health of subsequent generations [51].

This study, based on a large population sample, is the first study to reveal a significant association between SDoH, hyperuricemia, all-cause mortality, and cardiovascular mortality, and to analyze the mediating role of

SDoH in these relationships. The findings offer a new perspective on the complex impact of socio-economic factors on health outcomes and underline the importance of improving the social environment in reducing health risks associated with hyperuricemia. In addition to filling a research gap, this study provides robust evidence for public health interventions. The results suggest that offering greater health support can help reduce the risk of hyperuricemia and its associated mortality. Education-level improvements through community-based health literacy programs have been shown to enhance awareness of dietary risks and self-management of chronic conditions [52]. For instance, interventions combining nutritional education with practical cooking workshops reduced serum uric acid levels by 12% in low-income populations [53]. Additionally, addressing food insecurity requires multi-sectoral strategies. Subsidized access to low-purine foods in food deserts, combined with conditional cash transfers for healthy diets, significantly improved metabolic outcomes in a randomized trial [54].

Some limitations of this study should be considered when interpreting the results. Firstly, this study is based on a sample of adults residing in the United States, so the findings may not be fully applicable to populations in other countries or cultural settings. Secondly, the reliance on self-reported data for SDoH introduces the potential for memory bias. Moreover, this study does not account for competing risks, such as mortality from other causes, which may lead to biases in estimating cardiovascular mortality. Future research using competing-risks models could provide more accurate hazard ratios by adjusting for other causes of death. Additionally, this study does not examine the relationship between SDoH and unhealthy behaviors such as smoking and drinking, as well as their potential impact on the association between hyperuricemia and mortality. In future research, more comprehensive data and analytical methods should be employed to better explore this relationship. Finally, although this study discusses the associations between variables and the mediating effects, it cannot establish causality. The bidirectional effect between hyperuricemia and SDoH remains plausible, and determining the temporal order of these variables remains challenging. Future causal analysis and longitudinal studies are necessary to further explore the relationships between these variables.

Conclusions

This national cohort study revealed a significant positive association between SDoH, hyperuricemia, all-cause mortality, and cardiovascular mortality. Additionally, SDoH was found to play a substantial mediating role in the relationship between hyperuricemia and both all-cause and cardiovascular mortality. These results provide a novel perspective for the management of hyperuricemia and highlight the importance of improving socio-economic conditions and reducing adverse health factors as key strategies to reduce the mortality risk associated with hyperuricemia.

Abbreviations

SDoH	Social determinants of health
NHANES	National Health and Nutrition Examination Survey
PIR	Income-to-poverty ratio
NDI	National Death Index
NCHS	National Center for Health Statistics
BMI	Body mass index
CVD	Cardiovascular diseases
CDC	Centers for Disease Control and Prevention
MA	Mexican American
OH	Other Hispanic
NHW	Non-Hispanic White
NHB	Non-Hispanic Black
OR	Other Race
CRP	C-reactive protein
IL-6	Interleukin-6
XO	Xanthine oxidase

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

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Authors' contributions

ZW: Writing – original draft, Methodology, Investigation, Data curation, Formal analysis, Software. XC: Writing – original draft, Visualization, Investigation, Formal analysis. HC: Writing – review & editing, Investigation, Conceptualization. YW: Formal analysis, Methodology, Writing – review & editing. XT: Writing – review & editing, Supervision, Funding acquisition, Conceptualization. YQ: Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Conceptualization.

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Data availability

This study used publicly available data from NHANES, which can be accessed via the following link: https://www.cdc.gov/nchs/nhanes/.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Review Board of the National Center for Health Statistics (NCHS). All participants provided written informed consent prior to their involvement in the study.

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

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