International Journal for Vitamin and Nutrition Research

Int. J. Vitam. Nutr. Res. **2025**; 95(3): 36782
https://doi.org/10.31083/IJVNR36782

Original Communication

Dietary Selenium Intake and All-Cause Mortality in Diabetic Kidney Disease: A Dose-Response Relationship Based on the NHANES Observational Study

Xiaona Wang[1], Dongyan Wang[1], Shanshan Su[1,*]

[1]Department of Nephrology, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, 250014 Jinan, Shandong, China
*Correspondence: sushan8223@163.com (Shanshan Su)

Academic Editor: Torsten Bohn
Submitted: 5 January 2025 Revised: 27 April 2025 Accepted: 9 May 2025 Published: 1 July 2025

Abstract

Objective: Substantial experimental evidence has demonstrated that selenium, an essential micronutrient with pleiotropic physiological effects, also promotes dual antioxidant and anti-inflammatory effects. Meanwhile, the epidemiological association between dietary selenium consumption and mortality risk in diabetic kidney disease (DKD) remains underexplored. This investigation demonstrated a significant association between selenium intake and all-cause mortality among adult populations with DKD. **Methods**: This study analyzed data from 2183 individuals diagnosed with DKD, obtained from the National Health and Nutrition Examination Survey (NHANES) conducted between 2001 and 2014. The mortality rate was determined through linkage to the National Death Index until December 31, 2015. The hazard ratios (HRs) and their corresponding 95% confidence intervals (95% CIs) were calculated using Cox proportional hazards regression models. Kaplan–Meier survival curves were generated to examine the association between survival probabilities and selenium intake. **Results**: A total of 1063 mortalities were recorded over an average follow-up period of 8 years. All-cause mortality decreased with higher selenium intake levels. Adjusted for demographic variables, dietary habits, lifestyle factors, glucose regulation, and significant comorbidities, higher selenium intake was associated with improved all-cause mortality among DKD patients (adjusted HR = 0.705, 95% CI: 0.551–0.901). A significant overall association was observed between selenium intake and all-cause mortality risk, as evidenced by restricted cubic spline (RCS) analysis ($p_{\text{overall}} < 0.001$; $p_{\text{nonlinearity}} = 0.397$). **Conclusion**: Higher dietary selenium intake was significantly associated with lower risk of all-cause mortality after multivariable adjustment for confounders among individuals with DKD.

Keywords: nutritional epidemiology; diabetic kidney disease; all-cause mortality; selenium; micronutrients

1. Introduction

Diabetic kidney disease (DKD), formerly termed diabetic nephropathy, manifests as a diabetes-associated microvascular complication featuring elevated urinary protein excretion and reduced glomerular filtration rate [1]. DKD accounts for approximately 40% of diabetes-related renal complications in the U.S., imposing substantial public health burdens [2]. All-cause mortality rates in DKD patients are 30-fold higher than in diabetes patients without kidney impairment [3]. For the time being, strategies to delay DKD progression emphasize lifestyle modifications (e.g., diet, exercise) alongside pharmacotherapy to preserve renal function and glycemic control [4,5].

Discovered in 1817, selenium was long considered toxic until 1957 when studies revealed its role in preventing liver necrosis in rats, establishing its biological significance. As an essential trace element, bioavailable selenium supports critical physiological functions including nervous, endocrine, cardiovascular, and immune system regulation, and is linked to immune-related disorders. Natural dietary sources include grains, seafood, vegetables, and meats [6–8].

While selenium is essential for health, research has shown that chronic selenium intake exceeding the Tolerable Upper Intake Level (UL) may induce toxic effects, including hepatotoxicity, peripheral neuropathy, and dermatological/nail abnormalities (e.g., alopecia, nail dystrophy) [9]. Based on evidence from Selenium and Vitamin E Cancer Prevention Trial (SELECT) trial and other studies, the European Food Safety Authority established a UL of 255 µg/day for adults, including pregnant and lactating women [10]. Selenium exhibits an extremely narrow therapeutic window, with only a 3- to 5-fold difference between nutritional benefits and toxic doses [11,12]. This balance is particularly critical in diabetic kidney disease, where altered selenium metabolism may heighten toxicity risks.

Selenium regulates inflammation and immune responses through the cyclooxygenase/lipoxygenase pathway, and serves as a key component of antioxidant enzymes [13–16]. Deficiency in selenium is bound up with diabetes, cardiovascular diseases, autoimmune disorders, and cancer, particularly in developing countries [17]. Its antioxidant properties are recognized in type 2 diabetes pathophysiology and in mitigating oxidative stress linked to DKD [18–21]. By mimicking insulin action, reducing

insulin resistance, and enhancing glucose metabolism, selenium may offer beneficial effects for individuals with DKD [22]. Selenium exerts protective effects through selenoproteins, such as glutathione peroxidases (GPx), which mitigate oxidative stress by neutralizing reactive oxygen species (ROS) in renal tissues [23–25]. Aside from that, selenium modulates nuclear factor-kappa B signaling, reducing pro-inflammatory cytokines [e.g., interleukin-6 (IL-6); tumor necrosis factor-α (TNF-α)] that exacerbate renal fibrosis [26,27]. These mechanisms highly correspond with its potential to decelerate DKD progression and mortality. Studies have reported conflicting associations between blood selenium levels and diabetes incidence. Some suggest an inverse correlation with type 2 diabetes mellitus risk [28–30], while others indicate a positive association [31–34] or no significant link.

However, there is limited evidence regarding the direct impact of selenium on patients with DKD who are subject to heightened oxidative stress and inflammation, factors that elevate their risk of mortality. This study aims to fill these knowledge gaps by examining the association between selenium intake and all-cause mortality risk in a nationally representative cohort of DKD adults in the United States.

2. Research Design and Methods

2.1 Participants in the Study

The National Health and Nutrition Examination Survey (NHANES) database systematically compiles comprehensive health and nutrition data from a representative sample of the United States population. The database is updated biennially and is publicly accessible, enabling researchers to download the data for their studies. Participants' biological samples, such as blood and urine, are meticulously collected and analyzed. Additionally, the database encompasses numerous questionnaires encompassing demographic and socioeconomic factors, dietary and health concerns, as well as physical examinations that involve anthropometric measurements and laboratory assessments.

Data from NHANES 2001–2014 were utilized, which included information on selenium intake. Initially, individuals diagnosed with diabetes mellitus at baseline were included, creating a study group of 6536 participants. A physician's diagnosis, the use of insulin or oral medications to reduce blood sugar, or the consumption of insulin supplements characterized diabetes mellitus. Diagnosis was on the basis of a fasting blood sugar of $\geq$126 mg/dL, a 2-hour plasma glucose of 200 mg/dL or more following an oral glucose tolerance test, and a glycated hemoglobin A1c level of 6.5% or higher. DKD was identified by either a decreased estimated glomerular filtration rate, an albumin-to-creatinine ratio exceeding 30 mg/g, or both. A total of 2378 people met these criteria. After excluding 13 participants without survival data, 162 with missing dietary intake information, and 20 lacking other relevant covariates (Fig. 1), the final analysis included 2183 DKD participants (Fig. 1).

2.2 Assessment of Dietary Selenium Intake

Participants in the NHANES study underwent two 24-hour dietary recall interviews, the first conducted in person and the second via telephone 4–10 days later. Utilizing these two dietary recalls, the average selenium intake was calculated, with the analysis based on the Nutrients Database from the University of Texas Food Intake Analysis System [35]. Subsequently, the mean selenium intake was derived from the two recalls interviews.

2.3 Ascertainment of Mortality

Mortality status was ascertained using National Death Index records updated through December 31, 2015, with causes of death classified according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). codes. Cardiovascular disease deaths were identified by codes I00–I09, I11, I13, and I20–I51; cancer deaths were classified using codes C00–C97. The National Center for Health Statistics released the Public-Use Linked Mortality Files in 2015, which link to NHANES and span the years 1999–2014 [36]. These records provide detailed mortality status and underlying causes of death [37].

2.4 Assessment of Covariates

The surveys collected data on sociodemographic variables, smoking status, dietary patterns, diabetes medications, lipid-lowering therapies, and the presence of hypertension. Covariates were selected based on prior literature and biological plausibility. Directed acyclic graphs guided adjustments for confounders (e.g., age, HbA1c). Variance inflation factors were calculated to assess multicollinearity; all variance inflation factors (VIFs) were $<$5, indicating no severe collinearity (e.g., hemoglobin and iron: VIF = 4.8). A "never smoker" is defined as an individual who has smoked fewer than 100 cigarettes lifetime, while "current smokers" are those who have smoked more than 100 cigarettes and continue to smoke. In comparison, individuals who have ceased smoking after consuming more than 100 cigarettes are categorized as "former smokers". Hypertension was identified via self-report or measurement during the medical examination, defined as average systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg, or self-reported diagnosis. Participants who answered "YES" to the question, 'Have you ever been informed by a doctor or health professional that you had a stroke?' were classified as having experienced a stroke. The Dietary Inflammatory Index (DII) assesses the effects of 45 specific nutrients on inflammation [38]. The Systemic Immune-Inflammation Index (SII) is calculated by multiplying the total peripheral platelet count by the neutrophil-

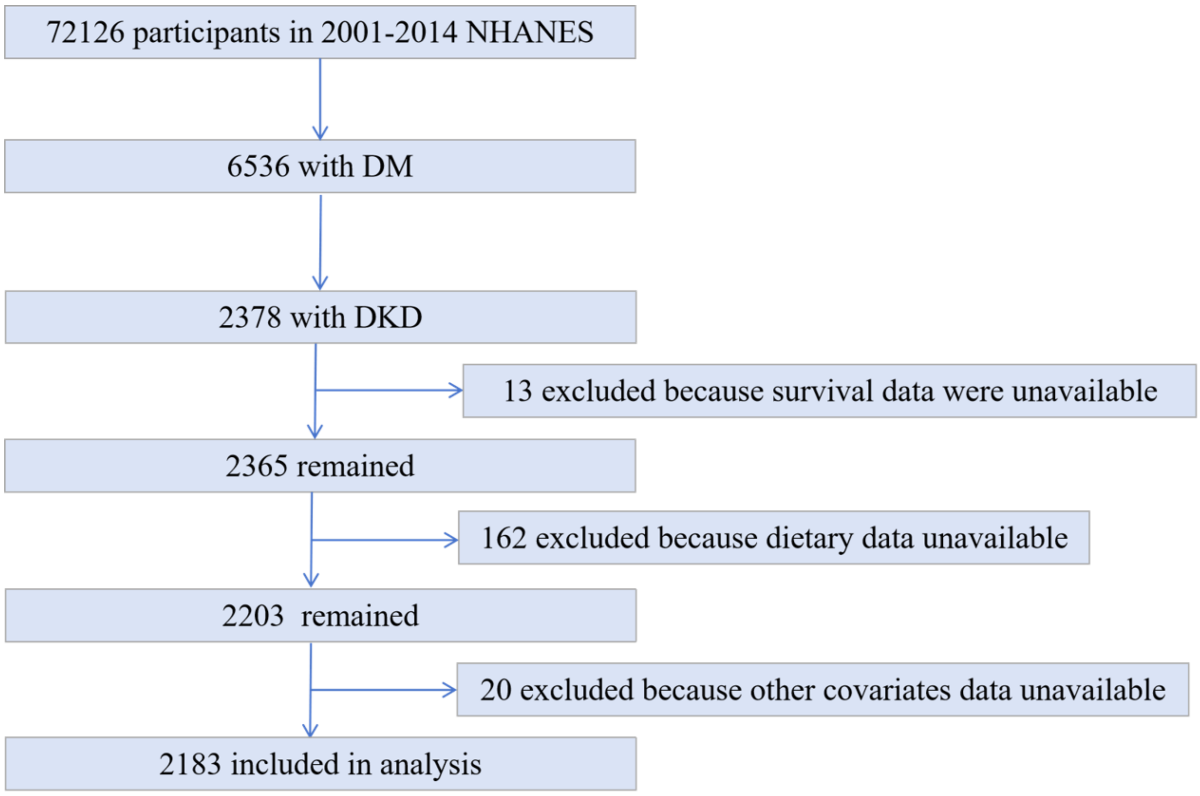

Fig. 1. Flow chart of sample selection from the National Health and Nutrition Examination Survey (NHANES) 2001–2014. DM, diabetes mellitus; DKD, diabetic kidney disease.

to-lymphocyte ratio. Blood cell counts were obtained using automated hematology analyzers and are reported as cells per microliter [39]. Additional information regarding these measurements is available in the NHANES Laboratory Medical Technologists Procedures Manual (https://wwwn.cdc.gov/nchs/nhanes/Default.aspx).

2.5 Statistical Analysis

The analyses incorporated sample weights, and participants were stratified into quartiles based on their selenium intake. Hazard ratios (HRs) and 95% confidence intervals were calculated using Cox proportional hazards regression. Models were adjusted for covariates in three sequential steps: Model 1 (unadjusted), Model 2 (demographic and inflammatory factors), and Model 3 (additional adjustments for glycemic control and renal function). Three models were utilized to compute HRs and 95% confidence intervals. The first model was subject to no adjustment. Model 2 was adjusted for sex, age, smoking status, family income-to-poverty ratio, hemoglobin levels, serum albumin levels, serum uric acid levels, dietary phosphorus intake, DII score, SII score, serum iron levels, and history of stroke. Model 3 was an extension of Model 2, further adjusted to include HbA1c, hypertension, hypoglycemic therapy, lipid-lowering therapy, and chronic kidney disease (CKD) stages defined by estimated glomerular filtration rate (eGFR): >60, 30–60, and <30 mL/min/1.73 m^2. The Kaplan-Meier plotter was employed to assess how dietary selenium consumption correlates with survival. A restricted cubic spline Restricted Cubic Spline (RCS) model with three knots was applied to explore associations between selenium intake and mortality, using the R package 'rms'. The analyses were conducted using R version 4.3.3 (https://www.r-project.org/), with statistical significance defined as $p < 0.05$.

3. Results

3.1 Subject Characteristics

Table 1 summarizes the baseline characteristics of 2183 participants with DKD (mean age 65.9 years; 53.4% male), stratified by quartiles of dietary selenium intake. The median selenium intake was 87.7 µg/day (interquartile range (IQR): 60.5–121.1 µg/day). Comparative analyses revealed significant differences across quartiles: higher selenium intake groups exhibited elevated hemoglobin (median Q4: 14.5 g/dL vs. Q1: 13.4 g/dL, $p < 0.0001$), serum iron (Q4: 79.0 µg/dL vs. Q1: 68.0 µg/dL, $p = 0.005$), and phosphorus intake (Q4: 1661 mg/day vs. Q1: 651 mg/day, $p < 0.0001$). Conversely, higher intake correlated with DII scores (Q4: 0.8 vs. Q1: 3.4, $p < 0.0001$). No significant trends were observed for age ($p = 0.06$), family income-to-poverty ratio ($p = 0.96$), or SII ($p = 0.12$). Mortality rates decreased progressively with higher selenium intake (Q1: 54.1% vs. Q4: 39.9%, $p < 0.001$).

Table 1. Baseline characteristics of participants by quartiles of selenium intake.

Characteristics	Total	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*p*
		<60.4 µg/d	60.5–87.6 µg/d	87.7–121 µg/d	>121 µg/d	
Patients, n	2183	547	545	545	546	
Age, year (%)						0.060
≤40	5.1	2.3	6.0	4.7	7.0	
40–60	26.1	23.4	28.0	25.8	27.0	
>60	68.8	74.3	66.0	69.5	66.0	
Male sex (%)	53.4	52.8	57.1	54.0	49.9	0.270
Race (%)						0.690
Non-Hispanic White	40.1	43.6	38.8	40.4	38.0	
Non-Hispanic Black	28.1	26.8	27.4	26.8	31.0	
Mexican American	18.5	17.2	19.8	17.3	19.5	
Other	13.3	12.4	14.0	15.5	11.5	
Family income-to-poverty ratio (%)						0.960
≤1	22.9	21.7	22.3	22.6	24.8	
1–3	52.8	54.4	52.5	52.3	52.1	
>3	24.3	23.9	25.2	25.1	23.1	
Smoking states (%)						0.340
Never smoker	45.0	48.8	43.9	42.7	44.7	
Former smoker	38.1	36.0	41.7	39.2	35.6	
Now smoker	16.9	15.2	14.4	18.1	19.7	
HbA1c, % (%)						0.002
≤7	48.5	58.1	47.6	46.4	42.6	
>7	51.5	41.9	52.4	53.6	57.4	
Stroke (%)	12.4	14.8	12.0	13.5	9.6	0.240
Hypertension (%)	80.9	80.2	84.4	82.8	76.6	0.070
HGB, g/dL	13.9 (12.6, 15.0)	13.4 (12.3, 14.7)	13.8 (12.5, 14.9)	12.7, 15.0	14.5 (13.1, 15.6)	<0.0001
ALB, g/dL	4.1 (3.9, 4.3)	4.1 (3.9, 4.3)	4.1 (3.9, 4.3)	4.1 (3.9, 4.3)	4.2 (3.9, 4.4)	0.050
UA, mg/dL	6.1 (5.0, 7.3)	6.2 (5.2, 7.3)	6.2 (5.2, 7.4)	6.0 (5.0, 7.2)	5.9 (4.9, 7.1)	0.150
Iron, µg/dL	74.0 (57.0, 96.0)	68.0 (53.0, 91.0)	75.0 (57.0, 99.0)	74.0 (56.0, 93.0)	79.0 (62.0, 101.0)	0.005
Phosphorus intake, mg/day	1082.0 (795.0, 1503.0)	651.0 (484.0, 868.0)	929.0 (769.0, 1119.0)	1204.0 (998.0, 1496.0)	1661.0 (1360.0, 2102.0)	<0.0001
Selenium intake, µ/d	89.6 (61.5, 124.6)	45.2 (33.6, 55.0)	73.4 (67.5, 80.1)	104.3 (96.3, 112.6)	154.1 (134.2, 184.5)	<0.0001
DII	2.2 (0.7, 3.2)	3.4 (2.3, 4.0)	2.7 (1.5, 3.4)	1.7 (0.6, 2.8)	0.8 (–0.5, 2.0)	<0.0001
SII	536.4 (378.3, 788.8)	561.0 (367.7, 825.9)	544.2 (396.1, 792.0)	542.8 (382.5, 805.2)	504.7 (352.4, 728.5)	0.120
Hypoglycemic treatment (%)	65.1	65.7	67.6	65.0	62.2	0.540
Lipid-lowering therapy (%)	90.1	88.4	93.9	89.9	88.3	0.050
Mortality (%)	47.4	54.1	51.2	45.2	39.9	<0.001

HGB, hemoglobin; ALB, albumin; UA, uric acid; DII, Dietary Inflammatory Index; SII, Systemic Immune-Inflammation Index.

The continuous variables in this study non-normally distributed and are thusreported as median (interquartile range [IQR]). Categorical variables are presented as %.

Table 2. Association between dietary selenium intake and all-cause mortality in DKD patients (NHANES 2001–2014).

Exposure	Quartiles of dietary selenium intake (µg/day)				*p* for trend
Range	Q1: <60.4 µg/d	Q2: 60.5–87.6 µg/d	Q3: 87.7–121 µg/d	Q4: >121 µg/d	
No. death/total	299/547	283/545	255/545	226/546	
Model 1	1 (reference)	0.817 (0.669, 0.998)	0.741 (0.611, 0.900)	0.610 (0.496, 0.749)	<0.001
Model 2	1 (reference)	0.810 (0.670, 0.979)	0.786 (0.628, 0.985)	0.714 (0.560, 0.909)	0.015
Model 3	1 (reference)	0.813 (0.669, 0.987)	0.789 (0.629, 0.989)	0.705 (0.551, 0.901)	0.021

Unless stated differently, data are presented as hazard ratio (HR) (95% CI).

Model 1: unadjusted model.

Model 2: adjusted for age (≤40, 40–60, >60years), sex (male or female), family income-to-poverty ratio (≤1.0, 1.0–3.0, or >3.0), smoking status (never smoker, former smoker, current smoker), hemoglobin (continuous), albumin (continuous), uric acid (continuous), dietary intake of phosphorus (continuous), Dietary Inflammatory Index (continuous), Systemic Immune-Inflammation Index (continuous), Serum iron (continuous), stroke (yes or no).

Model 3: Model 2 adjusted for additional variables: HbA1c (≤7%, >7%), hypertension (yes or no), hypoglycemic treatment (yes or no), lipid-lowering therapy (yes or no), chronic kidney disease (CKD) stages (estimated glomerular filtration rate (eGFR) categories: >60, 30–60, <30 mL/min/1.73 m^2).

3.2 Association Between Dietary Selenium Intake and All-Cause Mortality

Table 2 presents the all-cause mortality HRs for patients with DKD stratified by quartiles of selenium intake. In Model 1, which is unadjusted, the crude HRs (with 95% CIs) for mortality were observed across selenium intake categories of <60.4 µg/day, 60.5–87.6 µg/day, 87.7–121 µg/day, and >121.0 µg/day, with corresponding values of 1 (reference), 0.817 (0.669, 0.998), 0.741 (0.611, 0.900), and 0.610 (0.496, 0.749), respectively (p for trend < 0.001). In Model 2, after adjusting for age, sex, family income-to-poverty ratio, smoking status (never, former, current), hemoglobin, albumin, uric acid, dietary intake of phosphorus, DII, SII, serum iron, and stroke, the multivariate-adjusted HRs with 95% CIs for all-cause mortality were 1 (reference), 0.810 (0.670, 0.979), 0.786 (0.628, 0.985), and 0.714 (0.560, 0.909), respectively (p for trend = 0.015). Model 3 extended Model 2 by adding HbA1c, hypertension, hypoglycemic treatment, and lipid-lowering therapy, CKD stages, the multivariate-adjusted HRs with 95% CIs for all-cause mortality varied from 1 (reference) to 0.813 (0.669, 0.987), 0.789 (0.629, 0.989), and 0.705 (0.551, 0.901), indicating a significant trend (p trend = 0.021). Additionally, a restricted cubic spline analysis demonstrated a significant reduction in mortality risk with increasing selenium intake among patients with DKD (overall $p < 0.001$; nonlinear $p = 0.397$), as depicted in Fig. 2. Fig. 2A (untransformed hazard ratio, HR) shows a clear decline in mortality risk with increasing selenium intake, with the most pronounced reductions evident up to approximately 120 µg/day. Beyond this level, the hazard ratio stabilizes without evidence of further decline. Fig. 2B (log-transformed HR) further supports this negative association, displaying a uniform downward trend in Log-transformed hazard ratio (logHR) values as selenium intake rises, without suggesting curvature or reversal.

The Kaplan-Meier survival analysis in Fig. 3 demonstrates the relationship between dietary selenium intake and all-cause mortality. The risk table outlines the number of participants at risk and cumulative survival probabilities (in parentheses) across follow-up periods for each quartile (Q1: lowest, Q4: highest selenium intake). Survival curves for the highest intake group (Q4) exhibit higher survival probabilities compared with lower intake groups (Q1–Q3), indicating improved long-term survival. Log-rank test revealed significant differences across quartiles ($p < 0.05$). These results suggest a potential dose-dependent association between higher selenium intake and lower mortality risk.

Subgroup analyses revealed a consistent association between selenium intake and all-cause mortality when stratified by age >60 years, sex, Non-Hispanic Black individuals, eGFR >60 mL/min/1.73 m^2, and HbA1c (Table 3). No significant interactions were detected after adjusting for multiple testing. Among Non-Hispanic Black individuals in the highest selenium intake quartile (Q4), HR was significantly lower (HR = 0.444, 95% CI: 0.276–0.715) compared with other racial/ethnic groups.

4. Discussion

This study represents the first investigation into the relationship between dietary selenium intake and all-cause mortality among individuals with DKD. A significant dose-response relationship was identified between selenium intake and all-cause mortality. Importantly, this association remained independent of established risk factors, including diet and lifestyle, as well as interventions aimed at reducing blood glucose and lipid levels. Stratified analyses confirmed the robustness of our findings.

Our study identified a dose-dependent inverse association between dietary selenium intake and all-cause mortality in patients with DKD, a finding that aligns with the Invecchiare in Chianti (InCHIANTI) Study, where individuals in the lowest selenium quartile exhibited a 56%

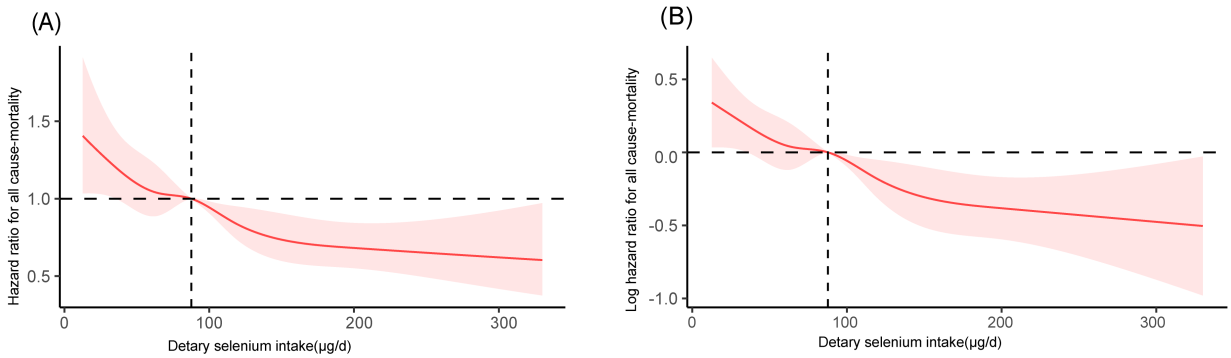

Fig. 2. Restricted cubic spline analysis of the association between dietary selenium intake and all-cause mortality in DKD patients (NHANES 2001–2014). (A) Untransformed hazard ratio (HR) with a reference line at HR = 1. (B) Log-transformed hazard ratio (logHR) with a reference line at logHR = 0 (equivalent to HR = 1). Both panels were adjusted for age, sex, family income-to-poverty ratio, smoking status, hemoglobin, albumin, uric acid, dietary phosphorus intake, Dietary Inflammatory Index (DII), Systemic Immune-Inflammation Index (SII), serum iron, stroke history, HbA1c, hypertension, hypoglycemic treatment, lipid-lowering therapy, and CKD stages. A median selenium intake of 87.7 μg/day was used as the reference. Shaded bands represent 95% confidence intervals. A significant overall association was observed ($p_{\text{overall}} < 0.001$), with no significant evidence of nonlinearity ($p_{\text{nonlinearity}} = 0.397$).

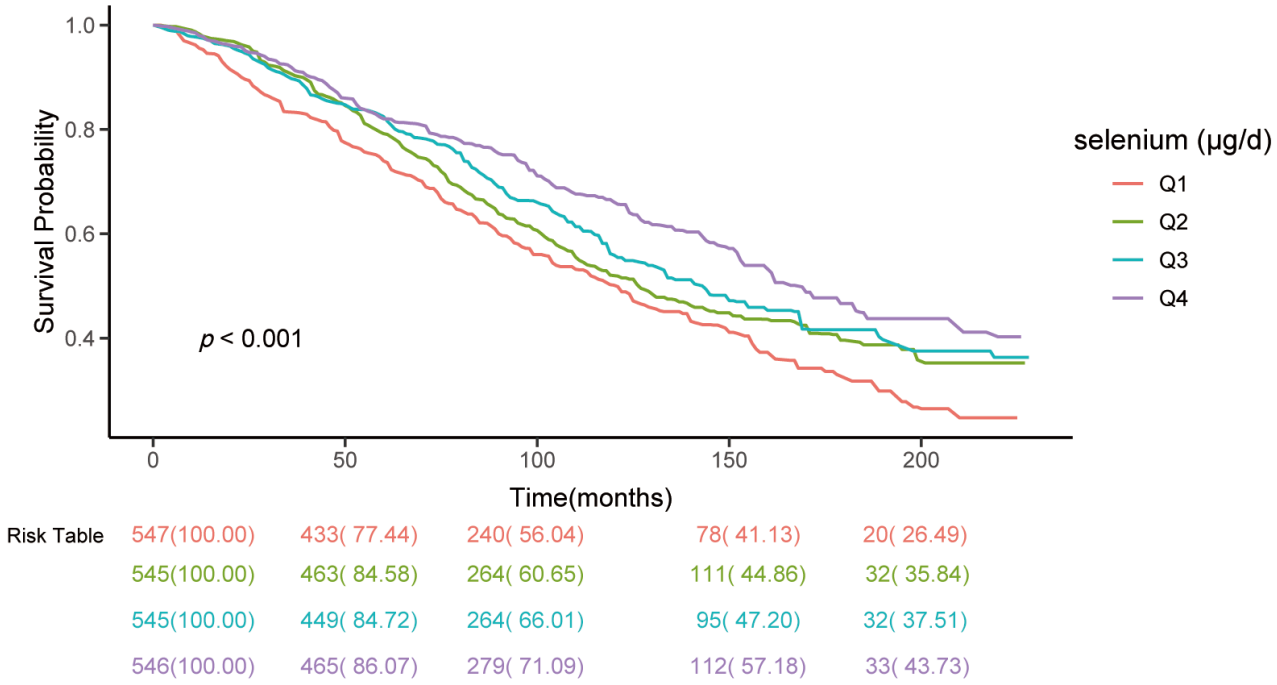

Fig. 3. Kaplan-Meier survival curves for all-cause mortality by quartiles of dietary selenium intake. Among individuals with DKD, those with a daily selenium intake of less than 60.4 μg/d exhibit the lowest cumulative survival probabilities, whereas individuals consuming more than 121.0 μg/d demonstrated significantly higher. log-rank test, $p < 0.005$. X-axis indicates follow-up duration in months.

higher mortality risk compared with those in the highest quartile [40]. However, our results contrast with a meta-analysis showing no significant mortality reduction with selenium supplementation in mixed populations [41], and diverge from a cohort of older adults reporting a U-shaped relationship between plasma selenium and mortality [42]. In contrast to prior studies in general or aging populations, our analysis exclusively targeted DKD patients—a high risk group characterized by increased oxidative stress and inflammation, where selenium's antioxidant and anti-inflammatory effects may exert stronger protective effects. While previous trials evaluated supplemental selenium (often in isolation), our study assessed dietary intake, reflecting real-world nutrient interactions and bioavailability.

Table 3. Stratified analyses of the association between dietary selenium intake and all-cause mortality among patients with DKD in NHANES 2001–2014.

Characteristic	Dietary selenium intake				*p* for trend	*p* interaction
	Quartile 1	Quartile 2	Quartile 3	Quartile 4		
Age, years						0.250
≤40 (n =114)	ref	0.349 (0.113, 1.078)	0.455 (0.148, 1.399)	0.459 (0.126, 1.666)	0.609	
40–60 (n = 520)	ref	0.529 (0.338, 0.826)	0.668 (0.393, 1.133)	0.404 (0.192, 0.853)	0.059	
>60 (n = 1549)	ref	0.918 (0.709, 1.189)	0.751 (0.570, 0.989)	0.688 (0.487, 0.973)	0.021	
Sex						0.532
Male (n = 1030)	ref	0.901 (0.700, 1.160)	0.710 (0.503, 1.004)	0.591 (0.393, 0.889)	0.009	
Female (n = 1153)	ref	0.716 (0.543, 0.945)	0.742 (0.543, 1.014)	0.619 (0.437, 0.876)	0.014	
Race/Ethnicity						0.898
Non-Hispanic White (n = 940)	ref	0.847 (0.625, 1.147)	0.799 (0.563, 1.134)	0.666 (0.408, 1.086)	0.109	
Non-Hispanic Black (n = 550)	ref	0.686 (0.481, 0.977)	0.649 (0.431, 0.977)	0.444 (0.276, 0.715)	0.002	
Mexican American (n = 398)	ref	0.929 (0.622, 1.387)	0.682 (0.346, 1.344)	0.737 (0.389, 1.396)	0.269	
Other (n = 295)	ref	0.769 (0.390, 1.514)	0.758 (0.313, 1.833)	0.905 (0.377, 2.174)	0.733	
HbA1c (%)						0.415
≤7.0 (n = 1254)	ref	0.797 (0.611, 1.040)	0.829 (0.645, 1.066)	0.588 (0.418, 0.827)	0.004	
>7.0 (n = 929)	ref	0.790 (0.553, 1.129)	0.640 (0.430, 0.952)	0.635 (0.403, 1.000)	0.037	
eGFR-EPI, mL/min/1.73 m^2						0.302
≤60 (n = 1095)	ref	0.763 (0.505, 1.151)	0.930 (0.623, 1.387)	0.731 (0.451, 1.184)	0.419	
>60 (n = 1088)	ref	0.926 (0.756, 1.135)	0.661 (0.503, 0.869)	0.629 (0.443, 0.893)	0.001	

The data are presented as HRs with 95% CIs, adjusted for various covariates including age (≤40, 40–60, >60 years), sex (male or female), family income-to-poverty ratio (≤1.0, 1.0–3.0, >3.0), smoking status (never, former, current), hemoglobin (continuous), albumin (continuous), uric acid (continuous), dietary phosphorus intake (continuous), DII (continuous), SII (continuous), serum iron (continuous), stroke history (yes or no), HbA1c levels (≤7%, >7%), hypertension (yes or no), hypoglycemic treatment (yes or no), and lipid-lowering therapy (yes or no), CKD stages (eGFR categories: >60, 30–60, <30 mL/min/1.73 m^2). It is important to note that the model did not incorporate the stratification variable when it was independently stratified. EPI, Chronic Kidney Disease Epidemiology Collaboration.

Dietary selenium primarily exists in organic forms, such as selenomethionine, which exhibit significantly higher bioavailability than inorganic selenium compounds. A study has demonstrated that the absorption efficiency of organic selenium exceeds 80% [43]. The bioavailability of selenium from dietary supplements, when co-ingested with food matrices, was determined to be within the range of 19.31%–66.10% [44]. Organic selenium enhances immunity through GPx synthesis, while excessive inorganic supplementation may inhibit immune function [45]. Prioritizing selenium-rich foods provides synergistic cofactors [43,46]. Public health strategies should emphasize 'dietary prioritization, targeted supplementation, and risk control', tailored to regional and population-specific characteristics [47].

The protective role of dietary selenium in reducing all-cause mortality among DKD patients may be mediated through multifaceted mechanisms targeting insulin resistance, oxidative stress, and inflammation-key drivers of DKD progression [48–51]. **(1) Improvement of Insulin Sensitivity and Metabolic Regulation.** GPx and thioredoxin reductases are selenium-dependent enzymes; thus, selenium deficiency induces oxidative damage to β-cells and impairs insulin secretion. These antioxidant enzymes, including selenoproteins, regulate cell differentiation and insulin secretion by affecting essential redox signaling [52, 53]. Selenium, as an integral component of antioxidative selenoproteins, plays a protective role against the onset of diet-induced insulin resistance in white adipose tissue by upregulating the expression of GPx3 and insulin receptors [54]. **(2) Attenuation of Oxidative Stress in Renal Cells.** In the renal ischemia-reperfusion injury model, selenium pretreatment significantly regulates the expression of multiple selenoprotein genes and alleviates oxidative stress-related renal injury [55,56]. This antioxidative action preserves glomerular filtration barrier integrity, thereby slowing the progression of albuminuria, a hallmark of early DKD. **(3) Suppression of NOD-like receptor protein 3 (NLRP3) Inflammasome-Mediated Inflammation.** Selenium exerts anti-inflammatory effects by suppressing NLRP3 activation via multiple pathways, such as upregulating GPx-1 to mitigate cadmium- or lipopolysaccharide-induced kidney injury via ROS-mediated NLRP3 suppression [57,58]. Nanoformulated selenium (e.g., Se@BSA nanoparticles) enhances renal targeting, inhibiting NLRP3 assembly, Caspase-1 activation, and IL-1β release in renal tubular cells [59]. Transcriptomic analyses identify GPX3 as a key selenoprotein that attenuates NLRP3 activity, highlighting selenium's dual antioxidative and anti-inflammatory roles [60].

In hierarchical analysis, Non-Hispanic Black individuals in the highest selenium intake quartile (Q4) revealed a strikingly lower HR (HR = 0.444, 95% CI: 0.276–0.715) in comparison with other racial/ethnic groups. This pronounced protective association may stem from a combination of genetic and dietary factors unique to this population. The metabolism of selenium is heavily influenced by genetic polymorphisms in selenoprotein-coding genes, such as those encoding selenoprotein P (*SEPP1*). For instance, SEPP1 is a key transporter of selenium in plasma, and functional variants in this gene (e.g., *rs7579*, *rs3877899*) have been demonstrated to alter selenium distribution and bioavailability [61]. Zhou *et al*. [62] reported that individuals with specific SEPP1 variants experienced differential lipid profile changes in response to selenium intake, suggesting gene-nutrient interactions may modulate health outcomes. Dietary patterns also play a crucial role in this process. Coastal or Southern U.S. populations, including a multitude of African American communities, traditionally consume higher amounts of selenium-rich foods such as fish, shellfish, and certain nuts. This dietary habit could maintain more stable selenium stores, optimizing its biological functions (e.g., glutathione peroxidase activity). Additionally, cultural food preparation methods (e.g., stewing or slow cooking) might preserve selenium bioavailability compared with processing techniques that degrade micronutrients.

Our findings suggest that optimizing selenium intake in DKD patients could reduce all-cause mortality risk. While current guidelines emphasize glycemic control and renoprotective agents, selenium supplementation may emerge as an adjunctive strategy. Future randomized trials should validate causality and define optimal dosing thresholds. From a clinical perspective, assessing selenium status (e.g., serum selenium levels) could help identify high-risk patients who may benefit from targeted interventions. Nevertheless, caution is warranted given potential toxicity at supranutritional intake levels.

In spite of the aforementioned contributions, the study's limitations involve numerous aspects, which are mirrored in its observational design, which precludes causal inference, and limited data on DKD severity, even after adjusting for diabetes medications and HbA1c levels. Data on diabetes duration in NHANES were insufficient to adjust for disease chronicity, a factor that may influence mortality outcomes. The findings are specific to U.S. adults enduring diabetes, thereby limiting generalizability. As suggested by the absence of genetic analysis on selenium metabolism, future research should explore diet-gene interactions affecting mortality. Moreover, the limited statistical power in subgroup analyses warrants cautious interpretation.

5. Conclusion

This study identified an association between increased dietary selenium intake and decreased mortality rates among patients with DKD. The findings suggest that selenium intake may offer mortality benefits for individuals with DKD.

Availability of Data and Materials

The study includes the original contributions, which are detailed in the article . For additional information, inquiries may be directed to the corresponding author.

Author Contributions

XW: Conducted data analysis and wrote the initial draft of the manuscript. DW and SS: Contributed to study conceptualization, research design, and critical revision of the manuscript. All authors reviewed and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Ethical approval was not required for this study, as it analyzed de-identified, publicly available data from the NHANES. NHANES protocols were approved by the National Center for Health Statistics Ethics Review Board, and all participants provided written informed consent prior to data collection. The study was carried out in accordance with the guidelines of the Declaration of Helsinki.

Acknowledgment

Not applicable.

Funding

This study was supported by Qilu Traditional Chinese Medicine Advantage Specialist Cluster Project and Shandong Traditional Chinese Medicine Technology Project (Grant Numbers: Z-2023062T, Q-2023014).

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Oshima M, Shimizu M, Yamanouchi M, Toyama T, Hara A, Furuichi K, *et al*. Trajectories of kidney function in diabetes: a clinicopathological update. Nature Reviews. Nephrology. 2021; 17: 740–750. https://doi.org/10.1038/s41581-021-00462-y.

[2] Doshi SM, Friedman AN. Diagnosis and Management of Type 2 Diabetic Kidney Disease. Clinical Journal of the American Society of Nephrology: CJASN. 2017; 12: 1366–1373. https://doi.org/10.2215/CJN.11111016.

[3] Sagoo MK, Gnudi L. Diabetic Nephropathy: An Overview. Methods in Molecular Biology (Clifton, N.J.). 2020; 2067: 3–7. https://doi.org/10.1007/978-1-4939-9841-8_1.

[4] Onyenwenyi C, Ricardo AC. Impact of Lifestyle Modification on Diabetic Kidney Disease. Current Diabetes Reports. 2015; 15: 60. https://doi.org/10.1007/s11892-015-0632-3.

[5] Wang J, Xiang H, Lu Y, Wu T, Ji G. New progress in drugs treatment of diabetic kidney disease. Biomedicine & Pharmacother-

apy = Biomedecine & Pharmacotherapie. 2021; 141: 111918. https://doi.org/10.1016/j.biopha.2021.111918.
[6] Roman M, Jitaru P, Barbante C. Selenium biochemistry and its role for human health. Metallomics: Integrated Biometal Science. 2014; 6: 25–54. https://doi.org/10.1039/c3mt00185g.
[7] Rayman MP. Selenium and human health. Lancet (London, England). 2012; 379: 1256–1268. https://doi.org/10.1016/S0140-6736(11)61452-9.
[8] Finley JW. Bioavailability of selenium from foods. Nutrition Reviews. 2006; 64: 146–151. https://doi.org/10.1111/j.1753-4887.2006.tb00198.x.
[9] Alexander J, Olsen AK. Selenium - a scoping review for Nordic Nutrition Recommendations 2023. Food & Nutrition Research. 2023; 67: 10.29219/fnr.v67.10320. https://doi.org/10.29219/fnr.v67.10320.
[10] Han F, Liu Y, Wang Q, Huang Z. Dietary Reference Intakes of Selenium for Chinese Residents. The Journal of Nutrition. 2025; S0022–S0022–3166(25)00014–8. https://doi.org/10.1016/j.tjnut.2025.01.008.
[11] Zambonino MC, Quizhpe EM, Mouheb L, Rahman A, Agathos SN, Dahoumane SA. Biogenic Selenium Nanoparticles in Biomedical Sciences: Properties, Current Trends, Novel Opportunities and Emerging Challenges in Theranostic Nanomedicine. Nanomaterials (Basel, Switzerland). 2023; 13: 424. https://doi.org/10.3390/nano13030424.
[12] Bai S, Zhang M, Tang S, Li M, Wu R, Wan S, *et al*. Effects and Impact of Selenium on Human Health, A Review. Molecules (Basel, Switzerland). 2024; 30: 50. https://doi.org/10.3390/molecules30010050.
[13] Tonelli M, Wiebe N, Bello A, Field CJ, Gill JS, Hemmelgarn BR, *et al*. Concentrations of Trace Elements and Clinical Outcomes in Hemodialysis Patients: A Prospective Cohort Study. Clinical Journal of the American Society of Nephrology. 2018; 13: 907–915. https://doi.org/10.2215/cjn.11451017.
[14] Yepes-Calderón M, Kremer D, Post A, Sotomayor CG, Seidel U, Huebbe P, *et al*. Low selenium intake is associated with risk of all-cause mortality in kidney transplant recipients. Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association - European Renal Association. 2023; 38: 2321–2329. https://doi.org/10.1093/ndt/gfad046.
[15] Liakopoulos V, Roumeliotis S, Bozikas A, Eleftheriadis T, Dounousi E. Antioxidant Supplementation in Renal Replacement Therapy Patients: Is There Evidence? Oxidative Medicine and Cellular Longevity. 2019; 2019: 9109473. https://doi.org/10.1155/2019/9109473.
[16] Rayman MP. The importance of selenium to human health. Lancet (London, England). 2000; 356: 233–241. https://doi.org/10.1016/S0140-6736(00)02490-9.
[17] Holben DH, Smith AM. The diverse role of selenium within selenoproteins: a review. Journal of the American Dietetic Association. 1999; 99: 836–843. https://doi.org/10.1016/S0002-8223(99)00198-4.
[18] González de Vega R, Fernández-Sánchez ML, Fernández JC, Álvarez Menéndez FV, Sanz-Medel A. Selenium levels and Glutathione peroxidase activity in the plasma of patients with type II diabetes mellitus. Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements (GMS). 2016; 37: 44–49. https://doi.org/10.1016/j.jtemb.2016.06.007.
[19] Yadav C, Manjrekar PA, Agarwal A, Ahmad A, Hegde A, Srikantiah RM. Association of Serum Selenium, Zinc and Magnesium Levels with Glycaemic Indices and Insulin Resistance in Pre-diabetes: a Cross-Sectional Study from South India. Biological Trace Element Research. 2017; 175: 65–71. https://doi.org/10.1007/s12011-016-0766-4.
[20] Wang XL, Yang TB, Wei J, Lei GH, Zeng C. Association between serum selenium level and type 2 diabetes mellitus: a non-linear dose-response meta-analysis of observational studies. Nutrition Journal. 2016; 15: 48. https://doi.org/10.1186/s12937-016-0169-6.
[21] Robertson RP, Harmon JS. Pancreatic islet beta-cell and oxidative stress: the importance of glutathione peroxidase. FEBS Letters. 2007; 581: 3743–3748. https://doi.org/10.1016/j.febslet.2007.03.087.
[22] Ezaki O. The insulin-like effects of selenate in rat adipocytes. The Journal of Biological Chemistry. 1990; 265: 1124–1128.
[23] Steinbrenner H, Sies H. Protection against reactive oxygen species by selenoproteins. Biochimica et Biophysica Acta. 2009; 1790: 1478–1485. https://doi.org/10.1016/j.bbagen.2009.02.014.
[24] Steinbrenner H, Speckmann B, Klotz LO. Selenoproteins: Antioxidant selenoenzymes and beyond. Archives of Biochemistry and Biophysics. 2016; 595: 113–119. https://doi.org/10.1016/j.abb.2015.06.024.
[25] Zachara BA. Selenium and selenium-dependent antioxidants in chronic kidney disease. Advances in Clinical Chemistry. 2015; 68: 131–151. https://doi.org/10.1016/bs.acc.2014.11.006.
[26] Youn HS, Lim HJ, Choi YJ, Lee JY, Lee MY, Ryu JH. Selenium suppresses the activation of transcription factor NF-kappa B and IRF3 induced by TLR3 or TLR4 agonists. International Immunopharmacology. 2008; 8: 495–501. https://doi.org/10.1016/j.intimp.2007.12.008.
[27] Gholizadeh M, Khalili A, Roodi PB, Saeedy SAG, Najafi S, Keshavarz Mohammadian M, *et al*. Selenium supplementation decreases CRP and IL-6 and increases TNF-alpha: A systematic review and meta-analysis of randomized controlled trials. Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements (GMS). 2023; 79: 127199. https://doi.org/10.1016/j.jtemb.2023.127199.
[28] Kljai K, Runje R. Selenium and glycogen levels in diabetic patients. Biological Trace Element Research. 2001; 83: 223–229. https://doi.org/10.1385/BTER:83:3:223.
[29] Kornhauser C, Garcia-Ramirez JR, Wrobel K, Pérez-Luque EL, Garay-Sevilla ME, Wrobel K. Serum selenium and glutathione peroxidase concentrations in type 2 diabetes mellitus patients. Primary Care Diabetes. 2008; 2: 81–85. https://doi.org/10.1016/j.pcd.2008.02.003.
[30] Thomas B, Ramesh A, Suresh S, Prasad BR. A comparative evaluation of antioxidant enzymes and selenium in the serum of periodontitis patients with diabetes mellitus type 2. Contemporary Clinical Dentistry. 2013; 4: 176–180. https://doi.org/10.4103/0976-237X.114867.
[31] Ekmekcioglu C, Prohaska C, Pomazal K, Steffan I, Schernthaner G, Marktl W. Concentrations of seven trace elements in different hematological matrices in patients with type 2 diabetes as compared to healthy controls. Biological Trace Element Research. 2001; 79: 205–219. https://doi.org/10.1385/BTER:79:3:205.
[32] Forte G, Bocca B, Peruzzu A, Tolu F, Asara Y, Farace C, *et al*. Blood metals concentration in type 1 and type 2 diabetics. Biological Trace Element Research. 2013; 156: 79–90. https://doi.org/10.1007/s12011-013-9858-6.
[33] Gao H, Hägg S, Sjögren P, Lambert PC, Ingelsson E, van Dam RM. Serum selenium in relation to measures of glucose metabolism and incidence of Type 2 diabetes in an older Swedish population. Diabetic Medicine: a Journal of the British Diabetic Association. 2014; 31: 787–793. https://doi.org/10.1111/dme.12429.
[34] Yerlikaya FH, Toker A, Arıbaş A. Serum trace elements in obese women with or without diabetes. The Indian Journal of Medical Research. 2013; 137: 339–345.
[35] Huang Y, Wei Y, Liang F, Huang Y, Huang J, Luo X, *et al*.

Exploring the link between dietary zinc intake and endometriosis risk: insights from a cross-sectional analysis of American women. BMC Public Health. 2024; 24: 2935. https://doi.org/10.1186/s12889-024-20433-9.

[36] Yin T, Cheang I, Zhu X, Liao S, Zhang H, Li X. The J-Curve Association Between Blood Pressure and Mortality in Stroke Survivors. International Journal of General Medicine. 2021; 14: 5039–5049. https://doi.org/10.2147/IJGM.S326301.

[37] Okedele OO, Nelson HH, Oyenuga ML, Thyagarajan B, Prizment A. Cytomegalovirus and cancer-related mortality in the national health and nutritional examination survey. Cancer Causes & Control: CCC. 2020; 31: 541–547. https://doi.org/10.1007/s10552-020-01296-y.

[38] Shivappa N, Steck SE, Hurley TG, Hussey JR, Hébert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutrition. 2014; 17: 1689–1696. https://doi.org/10.1017/S1368980013002115.

[39] Zhang Y, Meng Y, Chen M, Baral K, Fu Y, Yang Y, *et al*. Correlation between the systemic immune-inflammation indicator (SII) and serum ferritin in US adults: a cross-sectional study based on NHANES 2015-2018. Annals of Medicine. 2023; 55: 2275148. https://doi.org/10.1080/07853890.2023.2275148.

[40] Lauretani F, Semba RD, Bandinelli S, Ray AL, Ruggiero C, Cherubini A, *et al*. Low plasma selenium concentrations and mortality among older community-dwelling adults: the InCHIANTI Study. Aging Clinical and Experimental Research. 2008; 20: 153–158. https://doi.org/10.1007/BF03324762.

[41] Wang P, Chen B, Huang Y, Li J, Cao D, Chen Z, *et al*. Selenium intake and multiple health-related outcomes: an umbrella review of meta-analyses. Frontiers in Nutrition. 2023; 10: 1263853. https://doi.org/10.3389/fnut.2023.1263853.

[42] Bleys J, Navas-Acien A, Guallar E. Serum selenium levels and all-cause, cancer, and cardiovascular mortality among US adults. Archives of Internal Medicine. 2008; 168: 404–410. https://doi.org/10.1001/archinternmed.2007.74.

[43] D'Amato R, Regni L, Falcinelli B, Mattioli S, Benincasa P, Dal Bosco A, *et al*. Current Knowledge on Selenium Biofortification to Improve the Nutraceutical Profile of Food: A Comprehensive Review. Journal of Agricultural and Food Chemistry. 2020; 68: 4075–4097. https://doi.org/10.1021/acs.jafc.0c00172.

[44] Bawiec P, Sawicki J, Łasińska-Pracuta P, Czop M, Sowa I, Iłowiecka K, *et al*. In Vitro Evaluation of Bioavailability of Se from Daily Food Rations and Dietary Supplements. Nutrients. 2023; 15: 1511. https://doi.org/10.3390/nu15061511.

[45] Zhang J, Zhou H, Li H, Ying Z, Liu X. Research progress on separation of selenoproteins/Se-enriched peptides and their physiological activities. Food & Function. 2021; 12: 1390–1401. https://doi.org/10.1039/d0fo02236e.

[46] Wiesner-Reinhold M, Schreiner M, Baldermann S, Schwarz D, Hanschen FS, Kipp AP, *et al*. Mechanisms of Selenium Enrichment and Measurement in Brassicaceous Vegetables, and Their Application to Human Health. Frontiers in Plant Science. 2017; 8: 1365. https://doi.org/10.3389/fpls.2017.01365.

[47] Lentjes MAH. The balance between food and dietary supplements in the general population. The Proceedings of the Nutrition Society. 2019; 78: 97–109. https://doi.org/10.1017/S0029665118002525.

[48] Kamali A, Amirani E, Asemi Z. Effects of Selenium Supplementation on Metabolic Status in Patients Undergoing for Coronary Artery Bypass Grafting (CABG) Surgery: a Randomized, Double-Blind, Placebo-Controlled Trial. Biological Trace Element Research. 2019; 191: 331–337. https://doi.org/10.1007/s12011-019-1636-7.

[49] Ajjarapu AS, Hinkle SN, Li M, Francis EC, Zhang C. Dietary Patterns and Renal Health Outcomes in the General Population: A Review Focusing on Prospective Studies. Nutrients. 2019; 11: 1877. https://doi.org/10.3390/nu11081877.

[50] Man AWC, Li H, Xia N. Impact of Lifestyles (Diet and Exercise) on Vascular Health: Oxidative Stress and Endothelial Function. Oxidative Medicine and Cellular Longevity. 2020; 2020: 1496462. https://doi.org/10.1155/2020/1496462.

[51] Flemming NB, Gallo LA, Forbes JM. Mitochondrial Dysfunction and Signaling in Diabetic Kidney Disease: Oxidative Stress and Beyond. Seminars in Nephrology. 2018; 38: 101–110. https://doi.org/10.1016/j.semnephrol.2018.01.001.

[52] Casanova P, Monleon D. Role of selenium in type 2 diabetes, insulin resistance and insulin secretion. World Journal of Diabetes. 2023; 14: 147–158. https://doi.org/10.4239/wjd.v14.i3.147.

[53] Steinbrenner H, Duntas LH, Rayman MP. The role of selenium in type-2 diabetes mellitus and its metabolic comorbidities. Redox Biology. 2022; 50: 102236. https://doi.org/10.1016/j.redox.2022.102236.

[54] Hauffe R, Rath M, Agyapong W, Jonas W, Vogel H, Schulz TJ, *et al*. Obesity Hinders the Protective Effect of Selenite Supplementation on Insulin Signaling. Antioxidants (Basel, Switzerland). 2022; 11: 862. https://doi.org/10.3390/antiox11050862.

[55] Wu Y, Shi H, Xu Y, Wen R, Gong M, Hong G, *et al*. Selenoprotein Gene mRNA Expression Evaluation During Renal Ischemia-Reperfusion Injury in Rats and Ebselen Intervention Effects. Biological Trace Element Research. 2023; 201: 1792–1805. https://doi.org/10.1007/s12011-022-03275-7.

[56] Hasanvand A, Abbaszadeh A, Darabi S, Nazari A, Gholami M, Kharazmkia A. Evaluation of selenium on kidney function following ischemic injury in rats; protective effects and antioxidant activity. Journal of Renal Injury Prevention. 2016; 6: 93–98. https://doi.org/10.15171/jrip.2017.18.

[57] Candan B, Karakuyu NF, Gülle K, Sarman E, Ulusoy Karatopuk D. Beneficial Effects of Selenium on Kidney Injury via Nf-Kb and Aquaporin-1 Levels. Biological Trace Element Research. 2024; 202: 3653–3661. https://doi.org/10.1007/s12011-023-03928-1.

[58] Wang S, Chen Y, Han S, Liu Y, Gao J, Huang Y, *et al*. Selenium nanoparticles alleviate ischemia reperfusion injury-induced acute kidney injury by modulating GPx-1/NLRP3/Caspase-1 pathway. Theranostics. 2022; 12: 3882–3895. https://doi.org/10.7150/thno.70830.

[59] Zuo Z, Luo M, Liu Z, Liu T, Wang X, Huang X, *et al*. Selenium nanoparticles alleviate renal ischemia/reperfusion injury by inhibiting ferritinophagy via the XBP1/NCOA4 pathway. Cell Communication and Signaling: CCS. 2024; 22: 376. https://doi.org/10.1186/s12964-024-01751-2.

[60] Pei J, Tian X, Yu C, Luo J, Hong Y, Zhang J, *et al*. Transcriptome-based exploration of potential molecular targets and mechanisms of selenomethionine in alleviating renal ischemia-reperfusion injury. Clinical Science (London, England: 1979). 2023; 137: 1477–1498. https://doi.org/10.1042/CS20230818.

[61] Ferreira RR, Carvalho RV, Coelho LL, Gonzaga BMDS, Bonecini-Almeida MDG, Garzoni LR, *et al*. Current Understanding of Human Polymorphism in Selenoprotein Genes: A Review of Its Significance as a Risk Biomarker. International Journal of Molecular Sciences. 2024; 25: 1402. https://doi.org/10.3390/ijms25031402.

[62] Zhou L, Liang X, Xie M, Yin J, Huang Y, Li X, *et al*. A Functional Variant in *SEPP1* Interacts With Plasma Selenium Concentrations on 3-Year Lipid Changes: A Prospective Cohort Study. Frontiers in Nutrition. 2021; 8: 789577. https://doi.org/10.3389/fnut.2021.789577.