

## Postprint: Serum Uric Acid Levels and Risk of Chronic Kidney Disease Among Elderly in Longevity Areas of China

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### Abstract

**Background:** Elevated serum uric acid (SUA) leading to hyperuricemia (HUA) has been confirmed as an independent risk factor for the incidence and progression of chronic kidney disease (CKD); however, domestic cohort studies investigating the relationship between SUA levels and CKD occurrence and progression among the elderly remain scarce.

**Objective:** To examine the association of baseline SUA levels and their changes with the risk of CKD incidence and alterations in glomerular filtration rate among elderly individuals in Chinese longevity regions.

**Methods:** Drawing from the sub-cohort of the “Chinese Longitudinal Healthy Longevity Survey (CLHLS)” –the “Healthy Aging Biomarkers Cohort Study (HABCS)”, elderly subjects who underwent health examinations with biomedical indicators collected between 2012 and 2014 were enrolled. Biomedical parameters including age, sex, height, weight, waist circumference, calf circumference, blood pressure, blood lipids, blood glucose, and routine blood and urine indices were gathered at baseline and follow-up. Cox proportional hazards regression models were employed to analyze the association between different SUA levels and CKD incidence risk; Pearson linear correlation and linear regression analyses were utilized to assess the relationship between changes in SUA levels and eGFR changes in the elderly.

**Results:** A total of 981 subjects were included, with a mean age of  $80.1 \pm 11.9$  years. The prevalence of HUA was 6.83%, with cumulative follow-up of 2,029 person-years and median follow-up duration of 2.05 years. There were 179 incident CKD cases, yielding a cumulative CKD incidence of 18.25% (95%CI: 15.88-20.81%) during follow-up and an incidence density of 88.22/1,000 person-years (95%CI: 76.24-101.41 person-years). Following multivariate adjustment,

compared with the lowest quartile of baseline SUA (Q1 < 223 mol/L), the hazard ratios for CKD incidence risk in the higher quartiles (Q2 223-270 mol/L, Q3 271-326 mol/L, and Q4  $\geq$  326 mol/L) were 1.19 (95%CI: 0.74, 1.94; P=0.474), 1.27 (95%CI: 0.76, 2.10; P=0.362), and 2.08 (95%CI: 1.27, 3.41; P=0.004), respectively, with a trend of increasing risk (P for trend=0.003). Each 10 mol/L increase in baseline SUA level was associated with a 4% increase in CKD incidence risk (95%CI: 2%, 7%; P<0.001). Elderly individuals with HUA at baseline exhibited 2.00-fold higher risk of CKD incidence compared with those without HUA (95%CI: 1.20, 3.24; P=0.007). Pearson linear correlation analysis revealed that increasing SUA levels were associated with declining eGFR ( $r = -0.355$ , P<0.001). Multivariate-adjusted linear regression analysis indicated that each 10 mol/L increase in SUA level corresponded to a 1.03 ml/min/1.73m<sup>2</sup> decrease in eGFR (95%CI: -1.23, -0.83; P<0.001) during follow-up.

Conclusion: Elevated SUA levels in the elderly are associated with increased risk of new-onset CKD and decreased eGFR.

## Full Text

### Preamble

#### Association between Serum Uric Acid Level and the Risk of Chronic Kidney Disease among the Elderly in Longevity Areas in China

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### Abstract

**Background:** Hyperuricemia (HUA) caused by elevated serum uric acid (SUA) has been proven to be an independent risk factor for the development and progression of chronic kidney disease (CKD). However, there are few cohort studies on the correlation between SUA level and the development and progression of CKD in the Chinese elderly. **Objective:** To investigate the association between baseline SUA level, changes in SUA levels, the risk of CKD, and estimated glomerular filtration rate (eGFR) in the elderly in longevity areas in China. **Methods:** Based on the Healthy Aging and Biomarkers Cohort Study (HABCS), a sub-cohort of the Chinese Longitudinal Healthy Longevity Survey (CLHLS), the elderly who underwent physical examination and provided biomedical indicators from 2012 to 2014 were selected as the study subjects.

Age, gender, height, weight, waist circumference, calf circumference, blood pressure, blood lipids, blood glucose, blood routine examination, urine routine examination, and other medical indicators were collected at baseline and follow-up. Cox proportional hazards regression model was used to analyze the association between different SUA levels and the risk of CKD. Pearson linear correlation and linear regression were used to analyze the association between changes in SUA level and changes in eGFR in the elderly. **Results:** A total of 981 subjects were included in the study, with an average age of  $80.1 \pm 11.9$  years. The prevalence of HUA was 6.83%. The cumulative follow-up of 2029 person-years (median 2.05 years) showed 179 new cases of CKD, the cumulative incidence rate of CKD during the follow-up was 18.25% (95%CI: 15.88-20.81%), and the incidence density was 88.22/1000 person-years (95%CI: 76.24-101.41 person-years). After multivariate adjustment, compared with the lowest quartile group of baseline SUA level (Q1:  $<223$  mol/L), the HR values of CKD risk in the other three high quartile groups (Q2: 223-270 mol/L, Q3: 271-326 mol/L, and Q4  $\geq 326 \mu\text{mol/L}$ ) were 1.19 (95%CI: 1.02-1.38), 1.32 (95%CI: 1.15-1.51), and 1.45 (95%CI: 1.28-1.64), respectively. **Conclusion:** Elevated SUA level are associated with an increased risk of CKD and a decline in eGFR in an elderly Chinese population.

**Key words:** Chronic kidney disease; Serum uric acid level; Hyperuricemia; glomerular filtration rate; The elderly; Cohort study

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## Introduction

Chronic kidney disease (CKD) has become a major global public health threat. In China, the prevalence of CKD among adults aged 18 and above approaches 10.8%, affecting approximately 119 million individuals, yet the awareness rate in the general population remains only 12.5% [1]. Adults over 65 years represent the fastest-growing and largest group of end-stage renal disease patients [2,3]. As population aging intensifies in China, the incidence of CKD driven by chronic conditions such as hypertension, diabetes, and overweight/obesity continues to rise annually. Therefore, early identification and intervention of potential risk factors for CKD are crucial for preventing and delaying CKD progression and reducing complications in the elderly.

Serum uric acid (SUA), a product of purine nucleotide metabolism, is primarily excreted by the kidneys (approximately two-thirds) [4]. Hyperuricemia (HUA) caused by elevated SUA levels has been established as an independent risk factor for CKD development and progression [5-7]. Studies have shown that each 1 mg/dl increase in SUA level increases CKD risk by 19% [8], and uric acid-lowering therapy has demonstrated clinical benefits in slowing CKD progression [9]. However, some studies have reported inconsistent associations between elevated SUA and CKD risk [10,11]. Previous research has primarily analyzed the association between SUA levels and CKD risk in adult populations, while cohort studies focusing on the relationship between SUA levels and CKD development

in the Chinese elderly remain scarce.

Therefore, this study, based on the “Chinese Longitudinal Healthy Longevity Survey (CLHLS)” sub-cohort—the “Healthy Aging and Biomarkers Cohort Study (HABCS)” —aims to analyze the association between baseline SUA levels and their changes with CKD incidence risk and estimated glomerular filtration rate (eGFR) changes among elderly individuals in Chinese longevity areas, providing evidence for CKD prevention and management in this population.

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## Methods

### 1.1 Study Subjects

We selected 1,460 elderly individuals who underwent health examinations and provided biomedical indicators from 2012 to 2014 in the HABCS sub-cohort of CLHLS. Inclusion criteria were: (1) complete baseline SUA values; (2) complete baseline serum creatinine values; (3) complete baseline urinary microalbumin and urine creatinine values. Exclusion criteria were: (1) baseline eGFR  $<60$  ml/min/1.73m<sup>2</sup> (n=442); (2) baseline ACR  $\geq 30$  mg/g (n=23); (3) history of chronic nephritis (n=2); (4) lost to follow-up (n=12). This study was approved by the Ethics Committee of Tianjin Medical University General Hospital (IRB2022-WZ-118), and all participants provided informed consent.

### 1.2 General Information and Physical Examination Data Collection

We collected demographic characteristics, health status, and disease history (including hypertension, diabetes, kidney disease, and HUA) of the elderly participants. Physical measurements included height, weight, waist circumference, calf circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP), from which body mass index (BMI) was calculated.

### 1.3 Biomedical Indicator Detection

Medical staff collected 5 ml of venous blood for biochemical and routine blood tests, including fasting blood glucose (FBG), glycolated plasma protein (GSP), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum uric acid (SUA), serum creatinine (Scr), blood urea nitrogen (BUN), high-sensitive C-reactive protein (hs-CRP), vitamin D3 (25-oh-vitaminD3, VD3), superoxide dismutase (SOD), white blood cell count (WBC), red blood cell count (RBC), and platelet count (PLT). Midstream urine samples were collected for routine urinalysis and other urinary indicators, including urine protein, urine microalbumin (Ualb), and urine creatinine (Ucr), from which the albumin-to-creatinine ratio (ACR) was calculated.

#### 1.4 SUA Level Classification Standards

- (1) Participants were divided into quartile groups based on baseline SUA levels: Q1 <223 mol/L, Q2 223-270 mol/L, Q3 271-325 mol/L, and Q4  $\geq 326$  mol/L. (2) HUA was defined as baseline SUA level >420 mol/L in men or >360 mol/L in women, or a history of HUA [12].

#### 1.5 CKD Diagnostic Criteria

Based on the 2017 “Guideline for Screening, Diagnosis, Prevention and Treatment of Chronic Kidney Disease” and the National Kidney Foundation’s “Kidney Disease Outcomes Quality Initiative” [13,14], CKD was diagnosed when: (1) eGFR <60 ml/min/1.73m<sup>2</sup>; (2) or ACR  $\geq 30$  mg/g; (3) or newly diagnosed CKD based on medical records. eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation suitable for the Chinese population [15].

#### 1.6 Statistical Analysis

Statistical analysis was performed using Stata 13.0. Continuous variables with non-normal distribution were expressed as median (P25, P75), and between-group comparisons were made using Kruskal-Wallis H test. Categorical variables were expressed as frequency and proportion, with between-group comparisons using  $\chi^2$  test. Cox proportional hazards regression models were used to analyze the association between baseline SUA levels and CKD risk, with SUA quartile groups, SUA level (continuous variable), and HUA as independent variables and CKD incidence as the dependent variable, expressed as HR (95%CI). Trend tests were performed using median values of SUA quartile groups. Linear regression was used to analyze the association between baseline SUA level and baseline eGFR. Pearson linear correlation and linear regression were used to analyze the association between changes in SUA level ( $\Delta$ SUA = baseline SUA - follow-up SUA) and changes in eGFR ( $\Delta$ eGFR = baseline eGFR - follow-up eGFR). Model 1 was unadjusted; Model 2 was adjusted for age, gender, BMI, waist circumference, and calf circumference; Model 3 was further adjusted for SBP, DBP, FBG, GSP, TC, TG, HDL-C, LDL-C, hs-CRP, SOD, VD3, WBC, RBC, PLT, and BUN; Model 4 was further adjusted for history of hypertension and diabetes. All tests were two-sided, with P<0.05 considered statistically significant.

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## Results

### 2.1 Baseline Characteristics of Study Subjects

A total of 981 subjects were included, comprising 548 men (55.9%) with an average age of 80.1 $\pm$ 11.9 years. The prevalence of HUA was 6.83% (7.85% in

men, 5.54% in women;  $P=0.155$ ). The cumulative follow-up was 2029 person-years (median 2.05 years, range 1.0-4.0 years), during which 179 new CKD cases occurred. The cumulative incidence of CKD during follow-up was 18.25% (95%CI: 15.88-20.81%), with an incidence density of 88.22/1000 person-years (95%CI: 76.24-101.41 person-years).

Baseline characteristics including gender, BMI, waist circumference, calf circumference, SBP, GSP, TG, hs-CRP, VD3, WBC, PLT, BUN, Scr, Ucr,  $\Delta$ SUA,  $\Delta$ eGFR, and incident CKD differed significantly across SUA quartile groups (all  $P$ -values $<0.05$ ).

**Table 1 Baseline Characteristics of Study Subjects**

Characteristics	Q1 ( $n=245$ ) ( $<223$ )	Q2 ( $n=245$ ) (223-270)	Q3 ( $n=246$ ) (271-325)	Q4 ( $n=245$ ) ( $\geq 326$ )	$H/\chi^2$ value	$P$ value
Age (years)	80 (71, 90)	78 (70, 90)	79 (71, 88)	78 (71, 86)		
Male (n, %)	79 (32.24)	130 (53.06)	151 (61.38)	188 (76.73)		$<0.001$
BMI (kg/m <sup>2</sup> )	20.73 (18.67, 23.01)	21.41 (19.15, 23.83)	22.14 (19.84, 24.30)	22.75 (19.71, 25.65)	30.38	$<0.001$
Waist circumference (cm)	80 (72, 85)	80 (74, 88)	82 (76, 89)	83 (76, 91)		$<0.001$
Calf circumference (cm)	30 (27, 33)	30 (26, 33)	31 (28, 35)	32 (29, 35)		$<0.001$
SBP (mmHg)	130 (120, 150)	135 (120, 148)	140 (128, 154)	138 (126, 150)		
DBP (mmHg)	80 (73, 90)	80 (73, 90)	80 (73, 90)	80 (74, 90)		
FBG (mmol/L)	4.42 (3.85, 4.97)	4.32 (3.70, 4.88)	4.39 (3.60, 5.12)	4.50 (3.74, 5.21)		
GSP (mmol/L)	230.4 (213.2, 247.5)	232.2 (216.9, 245.7)	236.7 (219.6, 252.9)	235.8 (217.7, 257.4)	11.16	
TC (mmol/L)	4.20 (3.60, 4.94)	4.26 (3.68, 4.93)	4.30 (3.80, 5.08)	4.38 (3.76, 5.00)		

Characteristic	Q1 ( $<223$ ) (n=245)	Q2 (223-270) (n=245)	Q3 (271-325) (n=246)	Q4 ( $\geq 326$ ) (n=245)	$H/\chi^2$ value	$P$ value
TG (mmol/L)	0.76 (0.58, 1.05)	0.78 (0.56, 1.09)	0.86 (0.60, 1.21)	1.02 (0.68, 1.41)		$<0.001$
HDL-C (mmol/L)	1.26 (1.06, 1.49)	1.28 (1.05, 1.53)	1.26 (1.05, 1.53)	1.22 (1.03, 1.47)		
LDL-C (mmol/L)	2.51 (2.03, 2.99)	2.56 (2.02, 3.02)	2.56 (2.14, 3.11)	2.50 (2.06, 3.07)		
hs-CRP (mg/l)	0.60 (0.26, 1.49)	0.66 (0.33, 1.78)	0.69 (0.35, 1.59)	1.07 (0.52, 2.24)		$<0.001$
SOD (IU/ml)	56.94 (51.26, 61.84)	57.61 (52.93, 61.83)	56.27 (50.11, 61.26)	56.13 (51.59, 60.19)	6.00	
VD3 (ng/ml)	33.30 (25.77, 46.03)	40.70 (28.81, 50.70)	44.46 (32.44, 58.60)	48.96 (36.32, 61.69)	72.82	$<0.001$
WBC ( $10^9/L$ )	4.7 (4.0, 5.8)	5.2 (4.3, 6.3)	5.4 (4.6, 6.5)	5.5 (4.6, 6.8)		$<0.001$
RBC ( $10^{12}/L$ )	4.5 (4.0, 5.2)	4.4 (4.0, 5.3)	4.4 (4.0, 5.0)	4.4 (4.0, 5.0)		
PLT ( $10^9/L$ )	222 (159, 290)	213 (163, 277)	192 (150, 246)	178 (130, 230)		$<0.001$
BUN (mmol/L)	6.17 (5.15, 7.21)	6.13 (5.27, 7.39)	6.42 (5.17, 7.31)	6.39 (5.39, 7.52)		
Scr (mol/L)	62 (55, 69)	68 (61, 76)	75 (68, 83)	83 (74, 94)		$<0.001$
Ucr (mol/L)	1.57 (0.35, 6.83)	1.69 (0.31, 6.35)	1.82 (0.19, 6.25)	2.85 (0.45, 7.78)		
UAlb (mg/l)	82.06 (55.38, 120.49)	107.25 (63.95, 145.87)	115.24 (75.91, 152.77)	114.59 (75.26, 156.54)	37.06	$<0.001$
ACR (mg/g)	2.98 (0.50, 7.81)	1.93 (0.28, 7.10)	1.72 (0.23, 5.76)	2.12 (0.35, 6.69)		
$\Delta$ SUA (mol/L)	-28.15 (-58.15, -2.80)	-10.85 (-50.20, 20.90)	4.55 (-37.85, 35.50)	32.50 (-6.90, 79.40)	161.66	$<0.001$

	Q1 (<223) (n=245)	Q2 (223-270) (n=245)	Q3 (271-325) (n=246)	Q4 (\$ 326)(n = 245) H/ $\chi^2$ {2}	P
Characteristics				value	value
$\Delta$ eGFR (ml/min/1.73m <sup>2</sup> )	8.75 (-3.02, 20.36)	8.22 (-5.53, 19.18)	-0.18 (-8.62, 11.26)	-2.35 (-12.18, 8.25)	58.71
CKD (n, %)	53 (21.63)	49 (20.16)	66 (26.94)	69 (28.40)	
Hypertension (n, %)	5 (2.04)	4 (1.64)	5 (2.05)	7 (2.88)	
Diabetes (n, %)	40 (16.33)	37 (15.10)	42 (17.07)	60 (24.49)	

Note: SUA=serum uric acid, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure, FBG=fasting blood glucose, GSP=glycolated serum protein, TC=total cholesterol, TG=triglyceride, HDL-C=high-density lipoprotein cholesterol, LDL-C=low-density lipoprotein cholesterol, hs-CRP=high-sensitivity C-reactive protein, SOD=superoxide dismutase, VD3=vitamin D3, WBC=white blood cell count, RBC=red blood cell count, PLT=platelet count, BUN=blood urea nitrogen, Scr=serum creatinine, UAlb=urine microalbumin, Ucr=urine creatinine, ACR=albumin-to-creatinine ratio,  $\Delta$ SUA=change in serum uric acid,  $\Delta$ eGFR=change in estimated glomerular filtration rate, CKD=chronic kidney disease; Q1=<223 mol/L, Q2=223-270 mol/L, Q3=271-325 mol/L, Q4= $\geq$ 326 mol/L

## 2.2 Association between Different SUA Levels and CKD Risk in the Elderly

After multivariate adjustment, the results showed that as baseline SUA levels increased, CKD risk gradually increased. Compared with the lowest quartile group (Q1), the HR values for CKD risk in the higher quartile groups were 1.19 (95%CI: 0.74, 1.94; P=0.474), 1.27 (95%CI: 0.76, 2.10; P=0.362), and 2.08 (95%CI: 1.27, 3.41; P=0.004), respectively, with a significant trend (P-trend=0.003). For each 10 mol/L increase in baseline SUA level, CKD risk increased by 4% (95%CI: 2%, 7%; P<0.001). Compared with elderly without HUA at baseline, those with HUA had an increased CKD risk with an HR of 2.00 (95%CI: 1.20, 3.24; P=0.007). Linear regression analysis showed that baseline SUA level was negatively correlated with baseline eGFR ( $\beta$ =-0.897, SE=0.078, P<0.001).

### Table 2 Cox Proportional Hazard Regression Analysis of Different SUA Levels and the Risk of CKD in the Elderly

SUA level	HR (95%CI)	P-value	HR (95%CI)	HR (95%CI)	HR (95%CI)
	Model 1		Model 2	Model 3	Model 4
Q2	0.95 (0.61, 1.49)	0.496	1.19 (0.74, 1.94)	1.16 (0.75, 1.79)	1.18 (0.73, 1.92)
Q3	1.18 (0.74, 1.89)	0.269	1.27 (0.76, 2.10)	1.56 (0.98, 2.49)	1.33 (0.80, 2.20)
Q4	1.68 (1.13, 2.52)	<0.001	2.08 (1.27, 3.41)	2.53 (1.63, 3.93)	2.17 (1.33, 3.56)
Continuous variable a	1.03 (1.01, 1.05)	<0.001	1.04 (1.02, 1.07)	1.05 (1.03, 1.07)	1.04 (1.02, 1.07)
HUA	2.30 (1.48, 3.57)	<0.001	2.00 (1.20, 3.24)	2.20 (1.38, 3.50)	2.00 (1.22, 3.28)

Note: a Continuous variable, per 10 mol/L increase; Model 1, unadjusted; Model 2, adjusted for age, gender, BMI, waist circumference, calf circumference; Model 3, adjusted for SBP, DBP, FBG, GSP, TC, TG, HDL-C, LDL-C, hs-CRP, SOD, VD3, WBC, RBC, PLT, and BUN based on Model 2; Model 4, adjusted for history of hypertension and diabetes based on Model 3; Q1=<223 mol/L, Q2=223-270 mol/L, Q3=271-325 mol/L, Q4=≥326 mol/L

Pearson correlation analysis showed that as SUA levels increased, eGFR changes showed a decreasing trend ( $r = -0.355$ ,  $P < 0.001$ ) [Figure 1: see original paper]. After multivariate adjustment, linear regression results showed that for each 10 mol/L increase in SUA level, eGFR decreased by 1.03 (95%CI: -1.23, -0.83;  $P < 0.001$ ) ml/min/1.73m<sup>2</sup> during follow-up .

**Table 3 Linear Regression Analysis of Changes in SUA Level and Changes in eGFR in the Elderly**

Model	$\beta$ (95%CI)	P-value
Model 1	-1.404, -1.019	<0.001
Model 2	-1.412, -1.017	<0.001
Model 3	-1.228, -0.832	<0.001
Model 4	-1.226, -0.828	<0.001

Note: Model 1, unadjusted; Model 2, adjusted for age, gender, BMI, waist circumference, calf circumference; Model 3, adjusted for SBP, DBP, FBG, GSP, TC, TG, hs-CRP, HDL-C, LDL-C, SOD, VD3, WBC, RBC, PLT, BUN based on Model 2; Model 4, adjusted for history of hypertension and diabetes based on Model 3

**Figure 1 [Figure 1: see original paper]** Correlation between changes in SUA level and changes in eGFR among the elderly (A) overall, (B) male, (C) female

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## Discussion

This study, based on the HABCS sub-cohort of CLHLS, found that increased baseline SUA levels and HUA were associated with higher CKD risk and that eGFR declined as SUA levels increased.

Our results showed that the highest quartile group ( $\geq 326 \mu\text{mol/L}$ ) had 2.08 times (95% CI: 1.65-2.61) the CKD risk of the lowest quartile ( $< 5.1 \text{ mg/dl}$ ) [16]. WU et al. followed 4,546 volunteers for 4 years and found the highest SUA quartile ( $> 5.1 \text{ mg/dl}$ ) had 2.73 times (95% CI: 1.65-4.50) the CKD risk of the lowest quartile [17]. STORHAUG et al. found that each 1 mg/dl increase in baseline SUA increased renal insufficiency risk by 16% (95% CI: 4%-29%) after 13 years of follow-up [18].

We also found that baseline SUA level was negatively correlated with baseline eGFR, and each 10 mol/L increase in baseline SUA was associated with a 1.03 (95% CI: -1.23, -0.83) ml/min/1.73m<sup>2</sup> decline in eGFR during 4 years of follow-up. LAI et al. reported that each 1 mg/dl increase in baseline SUA was associated with a 1.25 (95% CI: -1.83, -0.67) ml/min/1.73m<sup>2</sup> eGFR decline over 3 years [16]. TSAI et al. showed that higher SUA levels were associated with significantly faster eGFR decline and higher renal failure risk, with each 1 mg/dl increase increasing progression to renal failure risk by 7% [19]. YE et al. also found that elevated SUA was independently associated with eGFR decline and increased CKD risk [20], all consistent with our findings.

Potential pathological mechanisms linking elevated SUA to increased CKD risk include: (1) The kidneys are the primary excretory organ for SUA, and uric acid crystals can deposit in the kidneys causing direct nephrotoxicity and reduced renal function [21]; (2) SUA absorbed by endothelial cells reduces nitric oxide (NO) levels by inhibiting production and accelerating degradation, while xanthine oxidase in cytoplasm and plasma produces superoxide that further reduces NO levels, thus elevated SUA induces intrarenal oxidative stress and mitochondrial dysfunction, damaging endothelial, smooth muscle, and tubular cells, and activating the renin-angiotensin system [22,23]; (3) HUA can induce pre-glomerular arteriolar lesions, impairing afferent arteriole autoregulation, while increased platelet adhesion and blood flow disturbances cause luminal occlusion and ischemia. Renal hypoperfusion is a potent vasoactive and inflammatory stimulus leading to tubulointerstitial inflammation and fibrosis [21,24], ultimately causing renal function decline.

This study has several limitations. First, the relatively small sample size of elderly participants may weaken the causal relationship between SUA levels and CKD risk. Second, using only single measurements of serum creatinine and proteinuria may introduce bias in assessing true CKD incidence in the elderly. Finally, the median follow-up of 2.05 years is relatively short, preventing observation of end-stage renal disease or renal death events; longer follow-up

is needed to validate these findings. Future studies should broaden endpoint observations and extend follow-up to continue monitoring CKD incidence in elderly populations.

In conclusion, elevated baseline SUA levels and HUA increase CKD risk and are associated with eGFR decline among elderly individuals in Chinese longevity areas. Regular monitoring of SUA levels and early intervention to control SUA are important for slowing future eGFR decline and reducing CKD development in the elderly.

**Author Contributions:** ZHANG Peng was responsible for data analysis and initial manuscript drafting; GAO Ying was responsible for study conception and overall article supervision; YANG Hongxi performed data analysis; WAN Chunxiao was responsible for quality control and manuscript review. All authors approved the final manuscript.

**Conflict of Interest:** All authors declare no conflict of interest.

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