Preplanned Studies

Association of Thallium Exposure with Decreased Renal Function among Chinese Adults — China, 2017–2018

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Summary

What is already known about this topic?

Thallium (Tl) is significantly more toxic than heavy metals such as lead, cadmium, and mercury. However, previous studies examining the relationship between Tl exposure and the risk of chronic kidney disease (CKD) have yielded inconsistent results.

What is added by this report?

The study demonstrated that elevated urinary Tl levels were associated with a higher prevalence of CKD and a reduced estimated glomerular filtration rate (eGFR), particularly among older adults. These findings were consistent in the restricted cubic spline (RCS) analyses.

What are the implications for public health practice?

This study identified Tl as a risk factor for decreased renal function, underscoring the need to enhance surveillance of Tl to mitigate the disease burden of CKD.

Thallium (Tl) is a highly toxic metal that has been designated as a priority environmental pollutant by the United States Environmental Protection Agency and included in China's 12th and 13th Five-Year Plans (*1*). While Tl is known to be nephrotoxic in cases of acute and subacute exposure, data on nephrotoxicity resulting from chronic exposure remain limited (*2*). The global incidence and prevalence of chronic kidney disease (CKD) have increased dramatically, making it a significant public health concern. In 2017, there were 697.5 million cases of CKD at all stages worldwide (*3*). Given China's large population, the economic and disease burden posed by CKD on both society and the national healthcare system are considerable (*4*). Consequently, extensive epidemiological studies are urgently needed to identify risk factors for CKD. Prior research has identified significant associations between Tl exposure and decreased kidney function (*5*–*6*), though the findings have not been consistent. This study investigates the association between urinary Tl and renal function, and further evaluates the potential mediating effect of inflammatory biomarkers, using data from the China National Human Biomonitoring (CNHBM) program.

In this study, participants younger than 18 years old and those with missing data on urinary Tl, serum creatinine (SCr), and inflammatory biomarkers were excluded. Following these exclusions, a total of 9,238 participants were included in the final analysis. The concentration of urinary Tl was measured using multi-element analysis via inductively coupled plasma mass spectrometry (ICP-MS) (PerkinElmer NexION 350, Turku, Finland).

This study utilized the Modification of Diet in Renal Disease (MDRD) equation to calculate the estimated glomerular filtration rate (eGFR), incorporating SCr, age, and gender. This method provides significant advantages in distinguishing various stages of CKD. The GFR measures the rate at which the glomeruli filter metabolites, waste, and toxins from plasma to produce ultrafiltrate, serving as a comprehensive indicator of kidney function. Clinical guidelines use eGFR for diagnosing and staging CKD, classifying eGFR values of less than 60 mL/[min·(1.73 m^2)] as indicative of CKD (*7*).

Continuous variables were presented as weighted mean (standard error, SE) or median (P_{25}–P_{75}), while categorical variables were represented as weighted percentages. Differences between continuous variables were assessed using analysis of variance or the rank sum test, depending on data distribution, and chi-square tests were employed for categorical variables. $P<0.05$ were considered statistically significant. Detailed definitions of covariates are provided in the Supplementary Material. The association between urinary Tl and CKD was examined using a multiple logistic regression model. Subsequently, a multiple

linear regression model was applied to estimate the regression coefficients (β) and 95% confidence interval (*CI*) of eGFR with respect to urinary Tl levels. A restricted cubic spline (RCS) with knots at the 25th, 50th, and 75th percentiles was utilized to explore dose-response relationships. To evaluate the role of inflammatory biomarkers, such as hypersensitive C-reactive protein (CRP), neutrophils, lymphocytes, and white blood cells (WBC), in the relationship between urinary Tl and eGFR, a mediation analysis was conducted using the mediation R package. Subgroup and sensitivity analyses were also performed, with detailed results available in the Supplementary Material (available at https://weekly.chinacdc.cn/).

The weighted median (P_{25}–P_{75}) of urinary Tl was 0.27 (0.16, 0.45) μg/L. The prevalence of CKD was 7.75%, and the weighted mean value of eGFR was 93.89 mL/[min·(1.73 m^2)]. Additional baseline characteristics of the participants are detailed in Supplementary Table S1 (available at https://weekly.chinacdc.cn/).

The highest quartile of urinary Tl was associated with an increased risk of CKD, exhibiting an adjusted odds ratio (*OR*) of 1.77 (95% *CI*: 1.04, 3.02) compared to the lowest quartile. Furthermore, for each additional interquartile range (*IQR*) of urinary Tl, the risk of CKD increased by 14% (*OR*=1.14, 95% *CI*: 1.02, 1.26) (Table 1). There was also a negative relationship between urinary Tl and eGFR, with a decrease in eGFR of 1.45 units (β=−1.45, 95% *CI*: −2.88, −0.02) for each unit increase in urinary Tl (Supplementary Table S2, available at https://weekly.chinacdc.cn/).

Urinary Tl exhibited a positive linear dose-response relationship with the risk of CKD within the RCS (*P* for linearity <0.05). Furthermore, RCS analysis indicated a negative downward dose-response association between urinary Tl and eGFR (*P* for linearity <0.05) (Figure 1).

Compared with the lowest quartile of urinary Tl, the second, third, and highest quartiles were all positively associated with the neutrophil ratio (*P*<0.05). Additionally, the third and highest quartiles of urinary Tl exhibited a negative relationship with the lymphocyte ratio (*P*<0.05) (Table 2). Each unit increase in the lymphocyte ratio corresponded with a 0.69 mL/[min·(1.73 m^2)] (95% *CI*: −1.30, −0.09) decrease in eGFR (Supplementary Table S3, available at https://weekly.chinacdc.cn/). However, mediation analysis results indicated no mediating role for the lymphocyte ratio in the association between Tl and eGFR (Supplementary Table S4, available at https://weekly.chinacdc.cn/).

Subgroup analyses stratified by gender and age group revealed a significant positive association between urinary Tl levels and CKD in women. Further examination by age indicated more pronounced positive effects in older adults (Supplementary Table S5, available at https://weekly.chinacdc.cn/). Sensitivity analyses, utilizing eGFR calculated via the CKD Epidemiology Collaboration (CKD-EPI) equation, corroborated these findings, demonstrating a stable association between urinary Tl levels and reduced renal function (Supplementary Table S6, available at https://weekly.chinacdc.cn/).

TABLE 1. Weighted odds ratios (95% *CI*) of CKD associated with urinary Tl concentration among Chinese adults in 2017–2018.

Urinary Tl	*OR* (95% *CI*)				
	Crude model	Model 1*	Model 2†	Model 3§	Model 4¶
Q1 (Reference)	1.00	1.00	1.00	1.00	1.00
Q2	0.93 (0.72, 1.20)	1.16 (0.88, 1.52)	1.14 (0.86, 1.50)	1.18 (0.90, 1.55)	1.14 (0.86, 1.51)
Q3	0.92 (0.66, 1.26)	1.27 (0.90, 1.80)	1.24 (0.87, 1.76)	1.29 (0.90, 1.87)	1.19 (0.81, 1.76)
Q4	1.51 (1.01, 2.24)**	2.08 (1.34, 3.24)**	1.99 (1.28, 3.10)**	2.09 (1.26, 3.48)**	1.77 (1.04, 3.02)**
Per *IQR*	1.14 (1.04, 1.24)**	1.19 (1.09, 1.30)**	1.18 (1.07, 1.29)**	1.19 (1.07, 1.31)**	1.14 (1.02, 1.26)**

Note: Q1=urinary Tl ≤0.16 μg/L; Q2=0.16 μg/L<urinary Tl≤0.28 μg/L; Q3=0.28 μg/L<urinary Tl≤0.46 μg/L; Q4=urinary Tl>0.46 μg/L.
Abbreviation: *CI*=confidence interval; CKD=chronic kidney disease; Tl=thallium; *OR*=odds ratio; *IQR*=interquartile range; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol; Cd=cadmium; Pb=lead; Hg=mercury; As=arsenic.
* Adjusted for age, sex, education, residence, marital status, and household income.
† Additionally adjusted for smoking status, drinking status, meat consumption, and vegetable consumption.
§ Additionally adjusted for hypertension, diabetes, BMI, UCr, and TC.
¶ Additionally adjusted for urinary Cd, urinary Pb, urinary Hg, and urinary As.
** *P*<0.05.

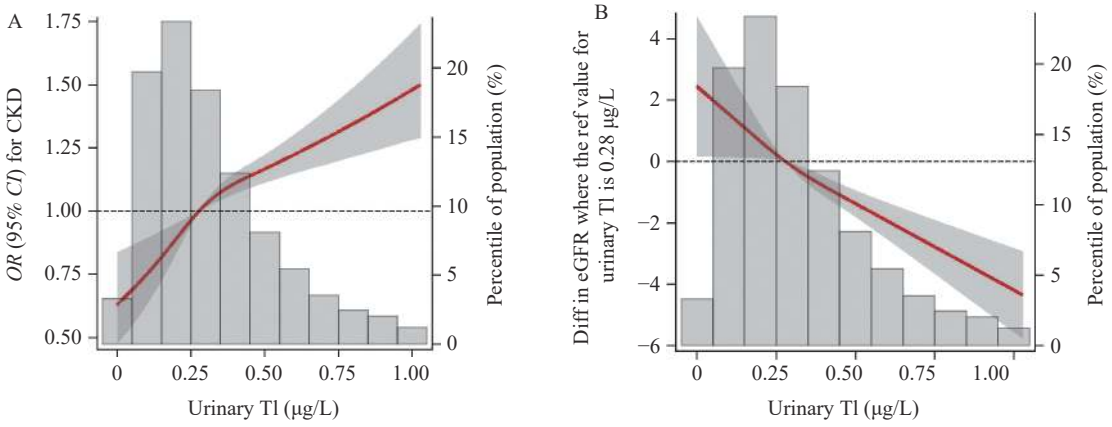

FIGURE 1. Restricted cubic spline for the association of urinary Tl with CKD and eGFR among Chinese adults in 2017–2018. (A) the dose-response relationship between urinary Tl and CKD; (B) the dose-response relationship between urinary Tl and eGFR.
Note: In the Figure 1A and 1B, the reference value was set at the 50th percentage of urinary Tl. Models were adjusted for age, sex, education, residence, marital status, household income, smoking status, drinking status, meat consumption, vegetable consumption, hypertension, diabetes, BMI, UCr, TC, urinary Cd, urinary Pb, urinary Hg, and urinary As.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval; Tl=thallium; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol; Cd=cadmium; Pb=lead; Hg=mercury; As=arsenic.

TABLE 2. Weighted regression coefficients (β) and 95% *CI* for the association of urinary Tl with inflammatory indicators among Chinese adults in 2017–2018.

Urinary Tl	β (95% *CI*)			
	CRP	Neutrophil ratio	Lymphocyte ratio	WBC
Q1 (Reference)	0	0	0	0
Q2	−0.30 (−0.74, 0.13)	1.06 (0.12, 2.30)*	0.59 (−2.44, 3.62)	0.07 (−0.14, 0.27)
Q3	0.08 (−0.50, 0.66)	1.13 (0.01, 2.25)*	−1.46 (−2.61, −0.32)*	0.06 (−0.11, 0.23)
Q4	−0.11 (−0.73, 0.52)	1.19 (0.09, 2.30)*	−1.26 (−2.44, −0.08)*	0.13 (−0.10, 0.36)
Per *IQR*	−0.07 (−0.19, 0.05)	0.37 (−0.01, 0.75)	−0.50 (−1.07, 0.08)	0.02 (−0.06, 0.10)

Note: Q1=urinary Tl≤0.16 μg/L; Q2=0.16μg/L<urinary Tl≤0.28 μg/L; Q3=0.28 μg/L<urinary Tl≤0.46 μg/L; Q4=urinary Tl>0.46 μg/L.
Abbreviation: *CI*=confidence interval; Tl=thallium; CRP=C−reactive protein; WBC=white blood cell count; *IQR*=interquartile range; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol.
Adjusted for age, sex, education, residence, marital status, household income, smoking status, drinking status, meat consumption, vegetable consumption, hypertension, diabetes, BMI, UCr, and TC.
* P<0.05.

DISCUSSION

Our study found a significant positive association between higher urinary Tl exposure and increased prevalence of CKD, as well as a decrease in eGFR. Notably, the positive associations with CKD were more pronounced in older adults.

The association between Tl and renal function remains inconclusive based on previous epidemiological studies. Urinary Tl has not been linked to an increased prevalence of CKD in the Chinese community of older adults in both single exposure and mixed metal exposure analyses (*8*). Conversely, a positive association has been reported between Tl and higher SCr- and cystatin-C-based eGFR in occupational populations, with the association persisting after adjustments for cadmium (Cd) and antimony (Sb) (*5*). Our study supports the hypothesis that Tl is associated with decreased renal function, aligning with a study in China that found significant impairment in kidney function among six children exposed to Tl (*6*). Discrepancies in results could be due to differences in participant characteristics, such as age and exposure concentrations. In our study, we adjusted for CKD risk factors, including hypertension, diabetes, total cholesterol (TC), BMI, and urinary metals, enhancing the robustness of our findings. We observed a stronger

association between Tl and CKD in women. Prior research has suggested that females may be more susceptible to kidney damage from heavy metals, possibly due to reduced estrogen production, which can diminish antioxidative capacity (*9*). A study in Taiwan, China, documented a decline in eGFR with age among subjects exposed to multiple metals (*10*). Our results are consistent with this finding, showing a higher risk of CKD in the 60–79 age group. The mechanism of Tl toxicity to the kidney remains incompletely understood. Animal studies have demonstrated nephrotoxic effects of Tl, with rat kidneys showing the highest accumulation of the metal (*11*). Previous research has indicated that high Tl exposure is associated with elevated CRP levels, suggesting that inflammation partly mediates effects of Tl on lung function (*12*). In this study, we identified an increased neutrophil ratio and a decreased lymphocyte ratio in individuals with high urinary Tl, indicating a positive association between Tl and inflammatory responses. Further in vivo and in vitro research is needed to explore the mechanisms underlying this relationship.

This cross-sectional study design limits our ability to determine the temporal relationship between exposure and outcome, introducing the risk of reverse causality. However, previous research using data from National Health and Nutrition Examination Survey (NHANES) has shown that as eGFR decreases, urinary Tl concentrations also decline, while urinary metal concentrations tend to rise with improved kidney function (*13*). These findings indicate that variations in renal function could affect urinary metal concentrations, potentially underestimating the true association between urinary metals and disease risk.

This study is subject to some limitations. First, urine microalbumin was not assessed, relying solely on eGFR for defining CKD, which could potentially underestimate the prevalence of CKD. Second, urinary Tl levels were measured using convenience samples rather than 24-hour urine collections, possibly introducing bias in estimating actual Tl exposure.

Tl exposure primarily occurs through the consumption of vegetables and potable water contaminated with Tl. Industrialization, along with the rapid development of mining and metal smelting, has exacerbated Tl contamination in surface water and soil. It is imperative to enhance monitoring of Tl levels in potable water, vegetables, and aquatic organisms, particularly in areas prone to Tl pollution such as those near Tl mining sites, thermal power plants, and metal smelting facilities. The current standards for Tl in surface and drinking water were established two decades ago and require urgent revision based on recent scientific findings. Moreover, existing toxicological data on both carcinogenic and non-carcinogenic effects of Tl are scarce, necessitating further research to better understand its potential health risks. Our study identified a significant link between Tl exposure and an increased risk of CKD and reduced eGFR, particularly among older adults. Given the critical issue of metal pollution, it is crucial to mitigate or eliminate renal toxic metal exposure to lessen the impact on renal function decline.

Conflicts of interest: Xiaoming Shi is an editorial board member of *China CDC Weekly* and was not involved in the peer review or handling of this manuscript. No other conflicts of interest.

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SUPPLEMENTARY MATERIALS

Methods

Study design: We utilized data from the China National Human Biomonitoring (CNHBM) project, a nationally representative biomonitoring initiative. CNHBM aims to establish baseline levels of internal exposure to environmental chemicals in the Chinese population and to monitor long-term trends. Employing a three-stage sampling design, CNHBM collected data from a total of 21,888 participants across 152 primary sampling units (PSUs) in 31 provinces of China between 2017 and 2018. Investigators from local county or district CDC offices conducted assessments of general household characteristics, household economic status, and sources of environmental chemical exposure using PSU and survey unit questionnaires. Details regarding sample collection, questionnaire survey, and physical examination have been previously documented (*1*). Ultimately, CNHBM recruited 21,746 participants. This study received approval from the ethics committees of the National Institute of Environmental Health, Chinese Center for Disease Control and Prevention (201701). All participants provided written informed consent.

Laboratory measurements: After an overnight fast of more than 8 hours, we collected 4 mL of heparinized blood, 12 mL of fasting blood without anticoagulants, and 80 mL of a single random urine sample in the morning. We diluted 0.5 mL of blood with a solution containing 0.1% nitric acid and 0.01% Triton X-100 and 1 mL of urine with 1% nitric acid, followed by centrifugation. The concentration of heavy metals in the urine was measured using inductively coupled plasma mass spectrometry (ICP-MS) (PerkinElmer NexION 350, Turku, Finland) with multi-element analysis. For quality control, parallel samples were analyzed simultaneously for every 30 samples. Spiked recoveries and relative standard deviations (RSD) were assessed at three concentration levels (2.5 μg/L, 5 μg/L, and 10 μg/L). The spiked recoveries of urinary Tl ranged from 87% to 98%, with RSD values within 9%. The limit of detection (LOD) for urinary Tl was 0.002 μg/L. For the 1.2% of urine samples below the LOD, 1/2 LOD values were imputed. Clinical biochemical parameters were measured using an automated biochemical analyzer (Hitachi 7180, Kyoto, Tokyo, Japan), including serum creatinine (SCr), fasting blood glucose (FBG), and total cholesterol (TC). Urine creatinine (UCr) levels were determined using picric acid spectrophotometry at local chemical laboratories.

Covariates: The covariates in our study were collected using standardized questionnaires administered by trained interviewers. The individual questionnaire gathered data on variables including age, sex (male or female), residence (rural or urban), education level (middle school or less, high school, or college or higher), marital status (married or not), alcohol consumption (yes or no), and smoking status (yes or no). Income was categorized into three groups: "<10,000 Chinese Yuan (CNY)," "10,000–100,000 CNY," and ">100,000 CNY." Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Dietary intake information was collected using a reliable and validated food frequency questionnaire (FFQ) designed specifically for the Chinese population, focusing on the dietary habits of subjects over the past year (*2*). Self-reported frequency of meat and vegetable consumption was classified into two categories: <14 and ≥14 times per week, using the median as the bisecting point. Participants were classified as having diabetes if they had a fasting serum glucose level of ≥7.0 mmol/L (126 mg/dL), a self-reported physician diagnosis of diabetes, or were currently taking insulin or oral hypoglycemic medications. Hypertension was defined as a systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg, a self-reported physician diagnosis, or current use of antihypertensive medication. Urinary concentrations of cadmium (Cd), mercury (Hg), lead (Pb), and arsenic (As) were included as covariates to account for the effects of other metals.

Subgroup analysis: We performed a subgroup analysis to examine the association effects across various demographics. Initially, we evaluated the relationship between Tl and CKD within different gender groups. Subsequently, a stratified analysis was conducted across distinct age categories (18–39, 40–59, 60–79) to delve deeper into these associations.

Sensitivity analysis: To validate the robustness of our results, we conducted multiple sensitivity analyses. We replicated the analysis using eGFR calculated with the CKD Epidemiology Collaboration (CKD-EPI) equation (*3*).

SUPPLEMENTARY TABLE S1. General characteristics among the Chinese population stratified by quartiles of urinary Tl concentration among Chinese adults in 2017–2018.

Characteristics	Total	Quartiles of urinary Tl				*P*
		Q1	Q2	Q3	Q4	
Age, mean±SE, year	47.52±0.25	49.55±0.57	47.11±0.48	46.28±0.40	47.21±0.47	<0.001
BMI, mean±SE, kg/m^2	24.52±0.12	24.55±0.18	24.70±0.20	24.41±0.14	24.41±0.13	0.444
eGFR, mean±SE, mL/[min·(1.73 m^2)]	93.89±1.68	94.52±2.40	95.52±1.92	94.69±1.71	90.61±2.12	<0.001
UCr, mean±SE, g/L	1.25±0.04	0.85±0.04	1.19±0.04	1.39±0.04	1.60±0.12	<0.001
TC, mean±SE, mmol/L	5.22±0.03	5.20±0.04	5.23±0.06	5.24±0.04	5.22±0.05	0.499
CRP, mean±SE, mg/L	2.16±0.09	2.27±0.20	1.95±0.09	2.29±0.19	2.16±0.23	0.036
Neutrophil ratio, mean±SE, %	58.34±0.32	57.82±0.41	58.55±0.40	58.43±0.56	58.54±0.44	0.729
Lymphocyte ratio, mean±SE, %	33.91±0.65	34.01±0.46	35.12±1.91	33.17±0.45	33.20±0.36	0.671
WBC, mean±SE, 10^9/L	6.13±0.05	5.99±0.08	6.14±0.09	6.16±0.07	6.24±0.10	0.006
Urinary Tl, median (P_{25}–P_{75}), μg/L	0.27 (0.16–0.45)	0.11 (0.07–0.13)	0.21 (0.18–0.24)	0.35 (0.31–0.39)	0.68 (0.55–0.93)	<0.001
Urinary Cd, median (P_{25}–P_{75}), μg/L	0.65 (0.32–1.32)	0.29 (0.14–0.57)	0.51 (0.30–0.95)	0.82 (0.49–1.41)	1.39 (0.75–2.50)	<0.001
Urinary Pb, median (P_{25}–P_{75}), μg/L	1.08 (0.61–1.72)	0.67 (0.32–1.22)	0.99 (0.61–1.59)	1.19 (0.45–1.79)	1.43 (0.94–2.18)	<0.001
Urinary Hg, median (P_{25}–P_{75}), μg/L	0.22 (0.10–0.48)	0.11 (0.04–0.21)	0.19 (0.10–0.37)	0.27 (0.15–0.58)	0.39 (0.21–0.80)	<0.001
Urinary As, median (P_{25}–P_{75}), μg/L	20.87 (11.32–40.13)	10.21 (5.73–19.00)	17.42 (10.44–31.27)	26.08 (15.19–44.67)	36.19 (22.27–61.78)	<0.001
Sex, No. (%)						0.002
Men	4,597 (37.94)	1,273 (43.50)	1,192 (36.44)	1,084 (36.15)	1,048 (35.91)	
Women	4,641(62.06)	966 (56.50)	1,196 (63.56)	1,210 (63.85)	1,269 (64.09)	
Educational, No. (%)						0.021
Middle school or less	5,836 (58.31)	1,511 (62.64)	1,517 (59.53)	1,343 (52.06)	1,465 (59.00)	
High school	1,872 (22.18)	417 (20.50)	472 (21.43)	489 (25.01)	494 (21.80)	
College or higher	1,530 (19.52)	311 (16.85)	399 (19.04)	462 (22.94)	358 (19.20)	
Residence, No. (%)						0.093
Rural	4,104 (37.26)	1,116 (42.39)	1,045 (36.02)	924 (33.92)	1,019 (36.93)	
Urban	5,134 (62.74)	1,123 (57.61)	1,343 (63.98)	1,370 (66.08)	1,298 (63.07)	
Marital status, No. (%)						0.144
Unmarried/divorced/widowed	1,506 (14.35)	396 (16.29)	418 (14.60)	374 (13.35)	318 (13.13)	
Married	7,732 (85.65)	1,843 (83.71)	1,970 (85.40)	1,920 (86.65)	1,999 (86.87)	
Annual income, No. (%)						<0.001
<10,000 CNY	1,367 (12.74)	431 (16.95)	369 (12.33)	297 (11.38)	270 (10.36)	
10,000–100,000 CNY	6,740 (72.51)	1,596 (71.26)	1,754 (74.78)	1,660 (70.29)	1,730 (73.51)	
>100,000 CNY	1,131 (14.75)	212 (11.79)	265 (12.88)	337 (18.33)	317 (16.14)	
Drinking status, No. (%)						0.235
No	5,254 (49.08)	1,360 (51.46)	1,391 (49.71)	1,243 (46.13)	1,260 (49.03)	
Yes	3,984 (50.92)	879 (48.54)	997 (50.29)	1,051 (53.87)	1,057 (50.97)	
Smoking status, No. (%)						0.309
No	6,594 (66.81)	1,700 (69.42)	1,721 (65.25)	1,593 (66.72)	1,580 (66.03)	
Yes	2,644 (33.19)	539 (30.58)	667 (34.75)	701 (33.28)	737 (33.97)	
Meat consumption, No. (%)						<0.001
<14 times/week	6,943 (75.57)	1,861 (81.92)	1,853 (78.21)	1,688 (74.00)	1,541 (67.85)	
≥14 times/week	2,295 (24.43)	378 (18.08)	535 (21.79)	606 (26.00)	776 (32.15)	

Continued

Characteristics	Total	Quartiles of urinary Tl				*P*
		Q1	Q2	Q3	Q4	
Vegetable consumption, No. (%)						<0.001
<14 times/week	3,036 (32.26)	835 (36.65)	868 (35.55)	727 (29.74)	606 (26.77)	
≥14 times/week	6,202 (67.74)	1,404 (63.35)	1,520 (64.45)	1,567 (70.26)	1,711 (73.23)	
Hypertension, No. (%)						<0.001
No	6,147 (65.09)	1,343 (58.45)	1,591 (67.53)	1,615 (67.88)	1,598 (66.16)	
Yes	3,091 (34.91)	896 (41.55)	797 (32.47)	679 (32.12)	719 (33.84)	
Diabetes, No. (%)						0.167
No	8,284 (89.01)	1,989 (88.36)	2,123 (87.39)	2,073 (89.89)	2,099 (90.59)	
Yes	954 (10.99)	250 (11.64)	265 (12.61)	221 (10.11)	218 (9.41)	
CKD, No. (%)						0.003
No	8,402 (92.25)	2,048 (92.78)	2,197 (93.24)	2,109 (93.34)	2,048 (89.50)	
Yes	836 (7.75)	191 (7.22)	191 (6.76)	185 (6.66)	269 (10.50)	

Note: Q1=urinary Tl≤0.16 μg/L; Q2=0.16 μg/L<urinary Tl≤0.28 μg/L; Q3=0.28 μg/L<urinary Tl≤0.46 μg/L; Q4=urinary Tl>0.46 μg/L. Results were weighted to account for the complex survey design.
Abbreviation: Tl=thallium; SE=standard error; BMI=body mass index; eGFR=estimated glomerular filtration rate; UCr=urine creatinine; TC=total cholesterol; CRP=C-reactive protein; WBC=white blood cell count; CKD=chronic kidney disease; Cd=cadmium; Pb=lead; Hg=mercury; As=arsenic; CNY=Chinese Yuan.

SUPPLEMENTARY TABLE S2. Weighted regression coefficients (β) and 95% *CI* for the association of urinary Tl with eGFR among Chinese adults in 2017–2018.

Urinary Tl	*β* (95% *CI*)				
	Crude model	Model 1*	Model 2†	Model 3§	Model 4¶
Q1 (Reference)	0.00	0.00	0.00	0.00	0.00
Q2	0.99 (−1.68, 3.67)	−0.55 (−3.31, 2.20)	−0.40 (−3.13, 2.33)	−0.37 (−3.16, 2.41)	−0.21 (−3.04, 2.62)
Q3	0.17 (−3.58, 3.91)	−1.91 (−5.68, 1.85)	−1.75 (−5.53, 2.04)	−1.58 (−5.44, 2.29)	−1.22 (−5.26, 2.82)
Q4	−3.91 (−9.31, 1.49)	−5.45 (−10.88, −0.01)**	−5.06 (−10.36, 0.23)	−4.78 (−10.21, 0.64)	−4.08 (−9.55, 1.39)
Per *IQR*	−1.58 (−3.10, −0.06)**	−1.81 (−3.33, −0.29)**	−1.70 (−3.16, −0.24)**	−1.64 (−3.10, −0.19)**	−1.45 (−2.88, −0.02)**

Note: Q1=urinary Tl≤0.16 μg/L; Q2=0.16 μg/L<urinary Tl≤0.28 μg/L; Q3=0.28 μg/L < urinary Tl≤0.46 μg/L; Q4=urinary Tl>0.46 μg/L.
Abbreviation: *CI*=confidence interval; Tl=thallium; eGFR=estimated glomerular filtration rate; *IQR*=interquartile range; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol; Cd=cadmium; Pb=lead; Hg=mercury; As=arsenic.
* Adjusted for age, sex, education, residence, marital status, and household income.
† Additionally adjusted for smoking status, drinking status, meat consumption, and vegetable consumption.
§ Additionally adjusted for hypertension, diabetes, BMI, UCr, and TC.
¶ Additionally adjusted for urinary Cd, urinary Pb, urinary Hg, and urinary As.
** *P*<0.05.

SUPPLEMENTARY TABLE S3. Weighted regression coefficients (β) and 95% *CI* for the association of inflammatory indicators with eGFR among Chinese adults in 2017–2018.

Variables	*β* (95% *CI*)			
	Crude model	Model 1*	Model 2†	Model 3§
CRP	−0.15 (−0.30, −0.00)	−0.05 (−0.18, 0.09)	−0.04 (−0.18, 0.10)	−0.04 (−0.18, 0.10)
Neutrophil ratio	−0.72 (−1.88, 0.45)	−0.25 (−1.28, 0.77)	−0.21 (−1.23, 0.82)	−0.30 (−1.29, 0.69)
Lymphocyte ratio	−0.27 (−1.00, 0.46)	−0.67 (−1.29, −0.05)¶	−0.73 (−1.31, −0.14)¶	−0.69 (−1.30, −0.09)¶
WBC	0.20 (−0.70, 1.09)	−0.33 (−1.07, 0.42)	−0.23 (−0.95, 0.50)	−0.24 (−0.97, 0.48)

Abbreviation: *CI*=confidence interval; eGFR=estimate glomerular filtration rate; CRP=C−reactive protein; WBC=white blood cell count; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol.
* Adjusted for age, sex, education, residence, marital status, and household income.
† Additionally adjusted for smoking status, drinking status, meat consumption, and vegetable consumption.
§ Additionally adjusted for hypertension, diabetes, BMI, UCr, and TC.
¶ *P*<0.05.

SUPPLEMENTARY TABLE S4. Mediating analysis of lymphocyte in the association of urinary Tl with eGFR among Chinese adults in 2017–2018.

Variable	ADE, *β* (95% *CI*)	*P*	ACME, *β* (95% *CI*)	*P*	Proportion of mediation, *β* (95% *CI*), %	*P*
Lymphocyte ratio	−2.00 (−2.43, −1.51)	<0.001	0.01 (−0.00, 0.02)	0.132	−0.40 (−1.22, 0.08)	0.132

Note: Adjusted for age, sex, education, residence, marital status, household income, smoking status, drinking status, meat consumption, vegetable consumption, hypertension, diabetes, BMI, UCr, and TC.
Abbreviation: Tl=thallium; eGFR=estimated glomerular filtration rate; ADE=average direct effect; ACME=average causal mediation effect; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol.

SUPPLEMENTARY TABLE S5. Weighted odds ratios (95% *CI*) of CKD associated with urinary Tl stratified by gender and age among Chinese adults in 2017–2018.

Groups		*OR* (95% *CI*)	*P*
Male		1.07 (0.93, 1.23)	0.352
Age group (years)	18–39	0.90 (0.48, 1.69)	0.734
	40–59	1.03 (0.84, 1.28)	0.756
	60–79	1.22 (0.97, 1.54)	0.086
Female		1.13 (1.01, 1.26)	0.029
Age group (years)	18–39	1.02 (0.84, 1.25)	0.840
	40–59	1.15 (1.00, 1.35)	0.054
	60–79	1.24 (1.05, 1.46)	0.012

Note: Adjusted for age, sex, education, residence, marital status, household income, smoking status, alcohol consumption, meat intake, vegetable intake, hypertension, diabetes, BMI, UCr, TC, urinary Cd, urinary Pb, urinary Hg, and urinary As.
Abbreviation: *CI*=confidence interval; CKD=chronic kidney disease; Tl=thallium; *OR*=odds ratio; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol; Cd=cadmium; Pb=lead; Hg=mercury; As=arsenic.

SUPPLEMENTARY TABLE S6. Associations between urinary Tl and CKD with eGFR calculated by CKD-EPI equation among Chinese adults in 2017–2018.

Urinary Tl	*β* (95% *CI*)				
	Crude model	Model 1*	Model 2†	Model 3§	Model 4¶
Q1 (Reference)	1.00	1.00	1.00	1.00	1.00
Q2	0.92 (0.66, 1.28)	1.21 (0.85, 1.72)	1.19 (0.84, 1.69)	1.21 (0.85, 1.72)	1.18 (0.82, 1.70)
Q3	0.92 (0.65, 1.31)	1.41 (0.97, 2.06)	1.39 (0.95, 2.03)	1.42 (0.96, 2.10)	1.34 (0.88, 2.04)
Q4	1.27 (0.84, 1.92)	1.89 (1.21, 2.96)**	1.83 (1.16, 2.87)**	1.87 (1.15, 3.05)**	1.61 (0.92, 2.79)
Per *IQR*	1.07 (0.98, 1.16)	1.15 (1.06, 1.24)**	1.14 (1.05, 1.23)**	1.14 (1.05, 1.23)**	1.09 (0.98, 1.20)

Note: Q1=urinary Tl≤0.16 μg/L; Q2=0.16 μg/L<urinary Tl≤0.28 μg/L; Q3=0.28 μg/L<urinary Tl≤0.46 μg/L; Q4=urinary Tl>0.46 μg/L.
Abbreviation: Tl=thallium; CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; *IQR*=interquartile range; BMI=body mass index; UCr=urine creatinine; TC=total cholesterol; Cd=cadmium; Pb=lead; Hg=mercury; As=arsenic.
* Adjusted for age, sex, education, residence, marital status, and household income.
† Additionally adjusted for smoking status, drinking status, meat consumption, and vegetable consumption.
§ Additionally adjusted for hypertension, diabetes, BMI, UCr, and TC.
¶ Additionally adjusted for urinary Cd, urinary Pb, urinary Hg, and urinary As.
** *P*<0.05.

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