BMC Nephrology

RESEARCH

Open Access

Association between serum uric acid variability and mild eGFR decline in Chinese adults: a retrospective cohort study

Na Li[1], Jianrong Wu[1], Jing Chen[1], Yajing Cui[1], Yunjie Teng[1] and Xiaoping Yang[1*]

Abstract

Background The present retrospective cohort study focused on evaluating the effects of fluctuations in serum uric acid (SUA) on a mildly reduced glomerular filtration rate (eGFR) in a population with a normal eGFR in Urumqi, China.

Methods A total of 2,154 normal individuals with a normal eGFR were recruited from 2018 to 2021. This study included questionnaire surveys, physical measurements, and blood sampling. We deemed the mildly reduced eGFR to be 60–90 $ml{\cdot}min^{-1}{\cdot}(1.73\ m^2)^{-1}$. The relationship between changes in SUA levels and the eGFR was assessed.

Results (1) During the 3-year follow-up period, 433 individuals (20.10%) presented mildly reduced eGFR. (2) After stratification by the degree to which uric acid changed into five groups, the group showing the greatest change in uric acid concentration had significantly lower eGFR values than the other four groups. As the uric acid concentration (ΔSUA) increased, the degree of mild eGFR reduction (ΔeGFR) also increased ($P < 0.05$). When classified into five groups by the degree of eGFR change (ΔeGFR), analysis of variance revealed no statistically significant differences between baseline SUA and follow-up SUA ($P > 0.05$). Pearson correlation analysis showed a negative correlation between ΔSUA and ΔeGFR ($r = -0.211$, $P < 0.01$). (3) Multifactorial logistic regression, in which the endpoint event was an eGFR decreasing to 60 to 90 $ml{\cdot}min^{-1}{\cdot}(1.73\ m^2)^{-1}$, revealed that the ΔSUA was a risk factor that independently predicted a reduced eGFR (OR = 1.347, $P < 0.001$).

Conclusion In people with a normal eGFR in Urumqi, a high SUA level is associated with a mild reduction in the eGFR.

Keywords Hyperuricemia, Serum uric acid, Estimated glomerular filtration rate, Chronic kidney disease (CKD)

*Correspondence:
Xiaoping Yang
yangxiaoping202209@163.com
[1]Health Management Center, First Affiliated Hospital of Xinjiang Medical University, No. 137, Lei Yue Shan South Road, Xincheng District, Urumqi, China

Introduction

Chronic kidney disease (CKD) is a globally prevalent and severe health condition that significantly impacts human quality of life and health. With increasing population aging, the incidence of CKD is gradually increasing, placing substantial pressure on healthcare systems [1–3]. Hyperuricemia (HUA), hypertension, and type 2 diabetes follow similar epidemiological trends [4–7] and are subjects of research as possible risk factors related to the occurrence of the aforementioned diseases. As reported in numerous studies, uric acid is related to renal function in CKD patients, and most patients typically seek medical attention only at the CKD stage. However, there are only a few reports on whether elevated uric acid levels are associated with a mild decrease in the eGFR in populations with normal kidney function, and most of these studies are cross-sectional. Existing research generally supports an affirmative viewpoint [8–10]. Previously, our research group conducted a correlation analysis of higher serum uric acid (SUA) levels in adults and rapidly declining renal function. The study revealed that increased uric acid levels independently predict the risk of rapidly declining renal function [11]. However, the role of uric acid in mildly reducing the eGFR among individuals with normal glomerular filtration rates has not been definitively established. The current study adopted a retrospective cohort design, with a focus on individuals with normal eGFR. This study analyzed how basic uric acid levels and alterations in these levels over a 3-year follow-up affected the estimated glomerular filtration rate (eGFR) to lay a certain theoretical foundation for health management in CKD individuals who are receiving routine medical examinations.

Study population and methods

Study population

This study utilized three consecutive years of follow-up data from the health examination population at the First Affiliated Hospital of Xinjiang Medical University in Urumqi, Xinjiang, China, starting in 2018. Patients who met the following criteria were included: (1) aged ≥ 20 years and (2) had resided in Urumqi for 6 months or longer. Patients with severe liver or kidney disease, habitual alcohol consumption, and those receiving medications for chronic kidney disease and hyperuricemia (e.g., ACE inhibitors, ARBs, corticosteroids, immunosuppressants, diuretics, traditional Chinese medicine and compound preparations for the treatment of chronic kidney disease, non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, IL-1 receptor antagonists, uricosuric agents, and uric acid synthesis inhibitors) were excluded. (2) Patients with a history of malignant tumors. (3) Patients whose eGFR are <90 ml·min^{-1}·(1.73 m^2)$^{-1}$ are excluded [12], as abnormal glomerular filtration rates may affect uric acid excretion. On the basis of the above criteria, we initially included 2,943 cases from the baseline data of 2018. Patients who died ($n=21$), were lost to follow-up ($n=763$), or had an eGFR <60 ml·min^{-1}·(1.73 m^2)$^{-1}$ during the 2021 follow-up ($n=5$) were excluded. The final study population consisted of 2,154 cases, ranging in age from 20 to 88 years. The Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University approved our study (Ethics Approval No: K202303–08).

Methods

Data extraction

Data from two serial health examinations for the study subjects, including age, sex, medical history, history of smoking, alcohol consumption and medication, family history, height, weight, heart rate, blood pressure, and other relevant parameters, were collected. Participants completed standardized epidemiological questionnaires onsite, addressing general information, relevant medical history, medication usage, and lifestyle factors (including smoking or drinking habits). Before initiating this work, the investigators received training and assessments, which included height, weight, and systolic and diastolic blood pressure measurements. The RG2–120 height and weight scale were used to measure participants' height and weight. After the participants sat quietly for at least 5 min, blood pressure measurement was completed with an electronic blood pressure monitor (GB3053–93) of the nondominant arm three times every minute to obtain the mean.

Laboratory examinations

After a fasting period of more than 10 h, blood (5 mL) was collected from the antecubital vein of each participant in the morning. This sample was then centrifuged to obtain the serum. Using an Olympus AU5811 (a fully automated biochemical analyzer from Olympus Corporation, Japan) and a Roche C800 automatic biochemical analyzer, various parameters, including total cholesterol, triglyceride levels, high- and low-density lipoprotein cholesterol (HDL-C and LDL-C, respectively), fasting blood glucose, creatinine, uric acid, alanine aminotransferase (ALT), blood urea nitrogen, and aspartate aminotransferase (AST), were assessed. All measurements were conducted with participants observing a minimum fasting period of 10 h.

Diagnostic definitions

Hyperuricemia was defined as SUA levels ≥ 7 mg/dL or ≥ 6 mg/dL in males and females, respectively [13, 14]. Moreover, we determined the eGFR via the CKD-EPI formula: eGFR $= 141 \times \min(\text{serum creatinine}/\kappa, 1)^{\alpha} \times \max(\text{serum creatinine}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$ (for females). Here, $\kappa = 0.7$ and $\alpha = -0.329$ for females, whereas

κ=0.9 and α=-0.411 for males. "min" indicates minimal serum creatinine/κ or 1, whereas "max" refers to maximal serum creatinine/κ or 1 [15]. A mildly reduced GFR was defined as an eGFR ranging from 60 to 90 ml·min^{-1}·(1.73 m^2)$^{-1}$ [12]. Additionally, we determined the body mass index (BMI) by dividing weight (kg) by height squared (m^2). Changes in uric acid levels (ΔSUA) were calculated by SUA_{2021} - SUA_{2018}, and the change in eGFR (ΔeGFR) was calculated as $eGFR_{2021}$- $eGFR_{2018}$. All subjects were classified into five groups on the basis of the change in uric acid (ΔSUA) level: $\Delta SUA_1 < -1.00$ mg/dL, ΔSUA_2 (−1.00 ~ −0.01) mg/dL, ΔSUA_3 (0.00 ~ 0.99) mg/dL, ΔSUA_4 (1.00 ~ 1.99) mg/dL, and $\Delta SUA_5 \geq 2.00$ mg/dL.(ΔeGFR) level: ΔeGFR1 < -20.00 ml·min^{-1}·(1.73 m^2)$^{-1}$, eGFR2 (-20.00 ~ -0.01)ml·min^{-1}·(1.73 m^2)$^{-1}$, ΔeGFR3 (0.00 ~ 9.99) ml·min^{-1}·(1.73 m^2)$^{-1}$, ΔeGFR4 (10.00 ~ 19.99) ml·min^{-1}·(1.73 m^2)$^{-1}$, and ΔeGFR5 ≥ 20.00 ml·min^{-1}·(1.73 m^2)$^{-1}$.

Statistical analysis

SPSS 27.0 was used for data analysis. For descriptive statistics, continuous variables with a normal distribution are represented by the mean ± standard deviation, whereas those with a nonnormal distribution are represented by the median (1st quartile, 3rd quartile). Nonparametric tests were employed to analyze data with a nonnormal distribution. Normally distributed continuous variables were compared by one-way analysis of variance (ANOVA) among different groups. Categorical variables are represented as frequencies or percentages and were compared via the chi-square test. Pearson's correlation analysis and logistic regression models were used for conducting correlation analyses. $P<0.05$ indicated a significant difference.

Results

Demographic characteristics

A total of 2,154 participants, aged 21–88 years, completed the 3-year follow-up in Urumqi city. The majority of the participants were males, comprising 1,397 cases (64.86%). In 2018, at baseline, the mean participant age was 41.16 ± 12.293 years. Among them, hyperuricemia was present in 187 individuals, and at the 3-year follow-up, 433 individuals (20.10%) experienced a mild decline in the eGFR. Statistically significant differences were detected ($P<0.05$) when sex, age, body mass index (BMI), systolic blood pressure, diastolic blood pressure, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine transaminase (ALT), aspartate transaminase (AST), blood urea nitrogen, serum uric acid (SUA), creatinine, and estimated glomerular filtration rate were compared between the hyperuricemia group and the normal uric acid group at baseline (Table 1).

Role of alterations in SUA levels in renal function

The data were classified into 5 groups according to alterations in SUA levels (ΔSUA), and analysis of variance

Table 1 Clinical information of the baseline and follow-up subjects in the normal uric acid and hyperuricemia groups

Variables	2018 Normal Uric Acid Group (*n* = 1967)	Normal Uric Acid Group After 3 Years of Follow-up (*n* = 1952)	2018 Hyperuricemia Group (*n* = 187)	Hyperuricemia Group After 3 Years of Follow-up (*n* = 202)
Female(n)	728	724	29[a]	33[b]
Age (year)	40.00(31.00,48.00)	44.36 ±12.269	36.00(30.00,43.00)[a]	42.27 ±12.324[b]
Body Mass Index (kg/m^2)	23.90 ±3.584	23.93 ±3.586	26.52 ±3.525[a]	26.41 ±3.500[b]
Systolic Blood Pressure (mmHg)	117.24 ±16.915	116.82 ±16.421	122.95 ±15.294[a]	123.91 ±15.442[b]
Diastolic Blood Pressure (mmHg)	75.25 ±11.865	75.03 ±11.366	80.37 ±11.242[a]	80.53 ±11.080[b]
Fasting blood glucose (mmol/L)	5.04 ±1.141	5.06 ±1.166	5.07 ±0.866	5.09 ±0.894
Total Cholesterol (mmol/L)	4.60(4.03,5.22)	4.68 ±0.909	4.75(4.06,5.57)	4.94 ±0.961[b]
Triglycerides (mmol/L)	1.20(0.84,1.80)	1.18(0.81,1.75)	1.90(1.26,2.84)[a]	1.94(1.31,2.83)[b]
High-Density Lipoprotein (mmol/L)	1.37 ±0.342	1.38 ±0.345	1.18 ±0.391[a]	1.21 ±0.312[b]
Low-Density Lipoprotein (mmol/L)	2.79(2.28,3.31)	2.81 ±0.755	2.96(2.40,3.59)[a]	3.09 ±0.768[b]
Alanine Aminotransferase (U/L)	18.30(12.90,27.50)	18.10(12.90,27.88)	30.50(20.20,48.60)[a]	28.95(19.20,45.05)[b]
Aspartate Aminotransferase (U/L)	19.00(15.80,27.50)	19.20(16.20,23.70)	23.00(18.10,30.30)[a]	22.50(18.10,28.78)[b]
Blood Urea Nitrogen (mmol/L)	4.60(3.81,5.50)	4.78 ±1.238	5.10(4.30,6.00)[a]	5.22 ±1.209[b]
SUA(mg/dL)	4.71(3.88,5.55)	4.71(3.92,5.57)	7.38(7.07,7.76)[a]	7.47(7.13,7.91)[b]
Creatinine (mmol/L)	66.00(56.96,75.00)	71.76(63.00,81.44)	76.00(68.00,83.00)[a]	83.23(76.00,92.00)[b]
eGFR	113.69 ±14.537	106.29 ±17.888	109.89 ±13.898[a]	99.22 ±17.234[b]
Number of Individuals with Mild eGFR Reduction (%)	0(0.0%)	367(84.76%)	0(0.0%)	66(15.24%)

Note SUA: serum uric acid; eGFR: estimated glomerular filtration rate; Comparison with the 2018 normal uric acid group [a]$P<0.05$; Comparison with the 3-year follow-up data of the normal uric acid group, [b]$P<0.05$

Table 2 Comparison of alterations in SUA levels with eGFR

ΔSUA	*N*	$eGFR_{baseline2018}$	$eGFR_{follow-up2021}$	ΔeGFR	Number of Individuals with Mild eGFR Reduction (%)
<-1.00	235	112.84 ±15.922	109.78 ±18.940	-3.05 ±15.996	36(15.3%)
-1.00–0.01	702	112.38 ±13.988	106.79 ±17.625[a]	-5.59 ±15.895[a]	121(17.2%)
0.00–0.99	967	113.56 ±14.524	104.89 ±17.548[a]	-8.68 ±14.505[ab]	205(21.2%)[ab]
1.00–1.99	206	114.35 ±14.801	102.39 ±18.577[a]	-13.96 ±15.994[abc]	56(27.1%)[ab]
≥ 2.00	44	113.49 ±11.922	96.56 ±16.644[abcd]	-16.93 ±18.948[abc]	15(34.1%)[abc]

Note SUA: serum uric acid; eGFR: estimated glomerular filtration rate; vs. <-1. 00, [a]*P*<0. 05; vs. −1. 00–0. 01, [b]*P*<0. 05; vs. 0. 00–0. 99, [c]*P*<0. 05; vs. 1. 00–1. 99, [d]*P*<0. 05, ΔSUA represents SUA_{2021}-SUA_{2018}, ΔeGFR represents $eGFR_{2021}$-$eGFR_{2018}$

Table 3 Comparison of eGFR changes with baseline uric acid, follow-up uric acid, and the number of individuals with mild eGFR reduction

ΔeGFR	*N*	$SUA_{baseline2018}$	$SUA_{follow-up2021}$	Number of Individuals with Mild eGFR Reduction (%)
<-20.00	452	5.18 ± 1.217	5.21 ± 1.262	234(54.0%)
-20.00–0.01	443	4.98 ± 1.266	5.06 ± 1.276	126(29.1%)a
0.00-9.99	646	4.89 ± 1.314	4.94 ± 1.317	73(16.9%)ab
10.00-19.99	525	5.00 ± 1.310	4.98 ± 1.368	0(0.0%)abc
≥ 20.00	88	4.98 ± 1.350	5.01 ± 1.392	0(0.0%)abc

Note SUA: Serum Uric Acid; eGFR: Estimated Glomerular Filtration Rate; vs.<Table 3 Comparison of Changes in Serum Uric Acid and eGFR <-20.00,[a]*P*<0. 05; vs. -20.00—0.01,[b]*P*<0. 05; vs0.00-9.99,[c]*P*<0. 05; vs. 1. 00–1. 99,[d]*P*<0. 05, ΔSUA为SUA_{2021}-SUA_{2018}, ΔeGFR为$eGFR_{2021}$-$eGFR_{2018}$

revealed that the eGFR at baseline was not significantly different ($P>0.05$). However, three years later, the group with the largest change in ΔSUA presented significantly lower eGFR values than did the other four groups. Additionally, eGFR values were significantly different among the ΔSUA_2, ΔSUA_3, and ΔSUA_4 groups ($P<0.05$). Further analysis of the correlation between ΔSUA (change in serum uric acid) and the degree of eGFR decline (ΔeGFR) revealed that with increasing ΔSUA, ΔeGFR also increased gradually. The extent of change in the ΔSUA_3, ΔSUA_4, and ΔSUA_5 groups markedly increased relative to that in the ΔSUA_1 and ΔSUA_2 groups ($P<0.05$). The chi-square test results indicated a noteworthy increase in the rate of mild eGFR decrease in the ΔSUA_5 group compared with the first three groups ($P<0.05$, Table 2). The participants were divided into five groups based on the degree of eGFR change (ΔeGFR), and variance analysis revealed no statistically significant differences in SUA levels between baseline and follow-up ($P>0.05$). Further analysis of the relationship between ΔeGFR and the number of individuals with mild eGFR reduction using a chi-square test showed that as ΔeGFR gradually decreased, the number of individuals with mild eGFR reduction significantly increased ($P<0.05$, Table 3). The correlation between ΔSUA and ΔeGFR was analyzed using the Pearson correlation method. The results showed a negative correlation between ΔSUA and ΔeGFR (r = -0.211, $P<0.01$, Fig. 1).

Logistic regression analysis of mild eGFR decline

When the eGFR decreased to 60–90 $ml{\cdot}min^{-1}{\cdot}(1.73\ m^2)^{-1}$ as an endpoint, we initially conducted univariate logistic regression to examine the relationships of influencing factors with a mild decrease in the eGFR. Additional adjustments were performed for age, sex, systolic blood pressure, diastolic blood pressure, body mass index, total cholesterol, triglycerides, HDL-C, LDL-C, fasting blood glucose, urea nitrogen, and baseline uric acid levels. Our results, even after these adjustments, continued to indicate that ΔSUA was a risk factor independently predicting mild eGFR decline (odds ratio [OR] = 1.347, $P<0.001$) (Table 4).

Discussion

Elevated blood uric acid levels are related to abnormal uric acid metabolism and reduced renal excretion. Uric acid crystal deposition can result in chronic inflammation in the renal arterioles and interstitial areas. Moreover, uric acid can induce microvascular damage in the afferent arterioles of the glomerulus, thus promoting CKD occurrence. A study conducted in Japan involving 48,177 adults tracked over a span of 7 years suggested that the risk of end-stage kidney disease significantly increased. The risk in men with SUA levels>7.0 mg/dL increased by 4-fold, whereas that in women with levels surpassing 6.0 mg/dL increased by 9-fold [16]. In a U.S. study involving individuals aged 65 years or older, when age, sex, baseline creatinine level, metabolic syndrome status, and diuretic use were adjusted, each 1 mg/dL increase in blood uric acid was related to an increase in kidney disease risk of 71% and a decrease in renal function risk of 14% (GFR decrease of 3 $ml{\cdot}min^{-1}{\cdot}(1.73\ m^2)^{-1}$) [17]. This study employed the CKD-EPI formula for determining the GFR [15]. In routine health assessments, kidney function indicators often rely on creatinine and uric acid levels, and the eGFR is rarely estimated for a more comprehensive evaluation of kidney function. Dynamic changes in kidney function were not considered. In this

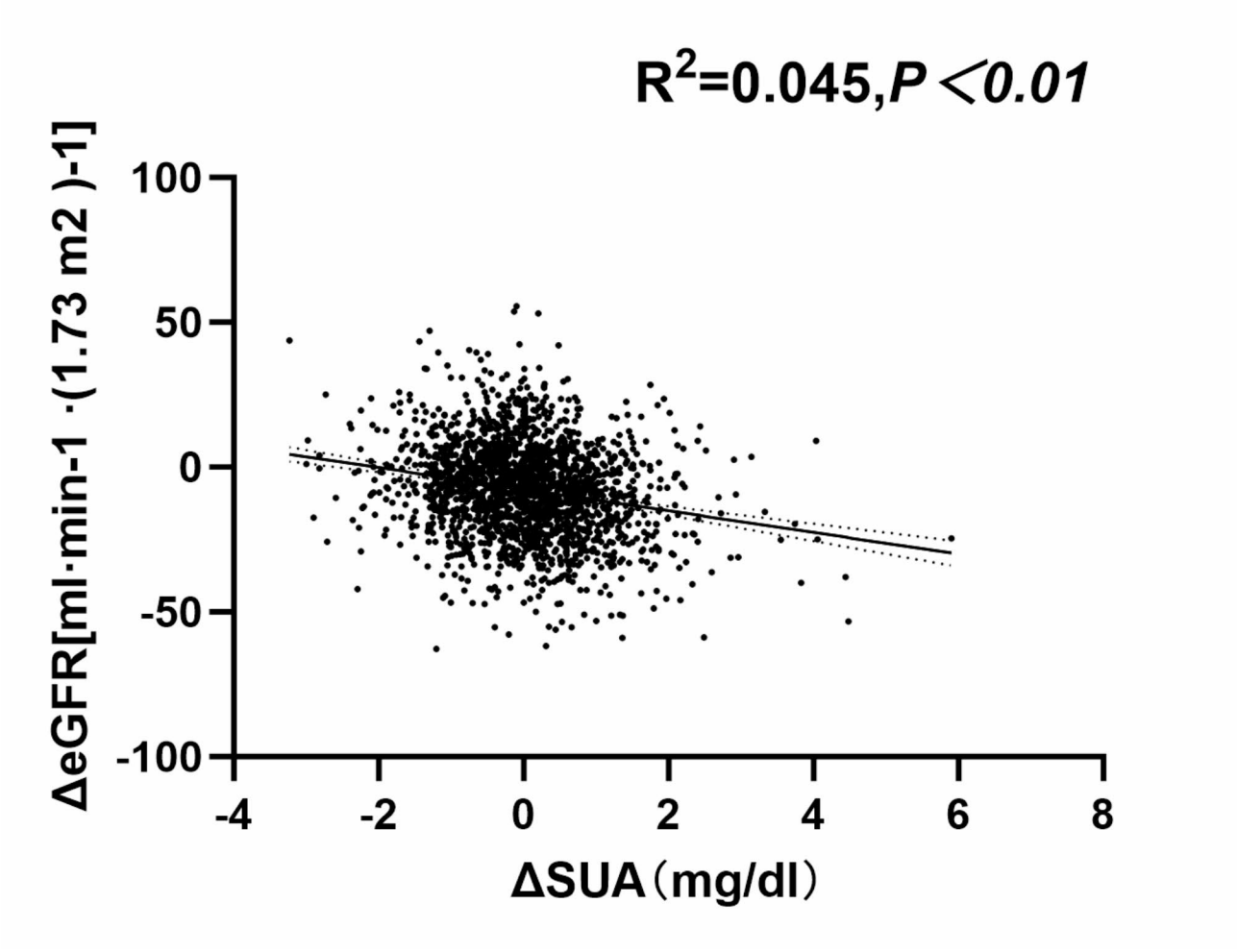

Fig. 1 Scatter plot of the correlation analysis of ΔSUA with ΔeGFR. *Note*: SUA: Serum uric acid; eGFR: Estimated glomerular filtration rate; ΔSUA represents SUA_{2021}-SUA_{2018}; ΔeGFR represents $eGFR_{2021}$-$eGFR_{2018}$

Table 4 Multifactorial logistic regression for eGFR decrease

variables	Univariate Regression			Multivariate Regression		
	Wald χ^2	*P*	OR (95% CI)	Wald χ^2	*P*	OR (95% CI)
Systolic Blood Pressure (mmHg)	26.221	< 0.001	1.016(0.010 ~ 1.022)			
Systolic Blood Pressure (mmHg)	24.487	< 0.001	1.331(1.189 ~ 1.491)			
Triglycerides (mmol/L)	14.201	< 0.001	1.179(1.084 ~ 1.283)			
High-Density Lipoprotein (mmol/L)	10.809	0.001	0.592(0.531 ~ 0.814)			
Low-Density Lipoprotein (mmol/L)	20.541	< 0.001	1.467(1.281 ~ 1.681)			
ΔSUA (mg/dL)	19.475	< 0.001	1.301(1.159 ~ 1.468)	23.190	< 0.001	1.347(1.193 ~ 1.522)

Note ΔSUA is defined as SUA_{2021} - SUA_{2018}. No factors were adjusted for in the univariate regression, whereas age, sex, systolic blood pressure, diastolic blood pressure, BMI, total cholesterol, triglycerides, HDL-C, fasting blood glucose, urea nitrogen, and baseline uric acid values were adjusted for in the multivariate regression

study, 433 individuals (20.10%) were identified as having experienced a mild decrease in eGFR. This highlights that regular screening and continuous assessment of the GFR are important, particularly for individuals undergoing routine health check-ups. The relationship between uric acid and kidney disease is well-established. In individuals with normal estimated glomerular filtration rate (eGFR), investigating the association between uric acid fluctuations and mild eGFR decline is critical for understanding potential early markers of renal dysfunction.

The present work involved a 3-year follow-up of the mentioned population, and a comparison of clinical data before and after the follow-up showed that with increasing age, the glomerular filtration rate (GFR) decreased. When the subjects were divided on the basis of their baseline blood uric acid level, the urea nitrogen and

creatinine levels tended to increase as the uric acid level increased, whereas the eGFR tended to decrease. Several studies have indicated a correlation between SUA levels and the occurrence of reduced GFR and renal dysfunction [18–20]. Our previous research also revealed that SUA levels are related to a rapid decline in renal function, which aligns with the conclusions drawn from our current study. A limitation of these studies is that renal function was assessed during follow-up solely on the basis of basic uric acid levels. Analyzing the correlation between baseline uric acid levels and renal function alone may overlook the actual fluctuations in uric acid levels and their impact on kidney function. Hence, this study employed the extent of uric acid change, defined as the difference between follow-up and baseline SUA, and the degree of glomerular filtration rate decline, represented by the difference between baseline and follow-up eGFR, to conduct a more detailed investigation into the impact of uric acid fluctuations on mild eGFR reduction. The degree of change in uric acid content can be divided into five groups. Our results indicated that at baseline, the GFR was not significantly different across diverse groups. However, at follow-up, the group with the highest degree of uric acid change (>2.00 mg/dL) not only experienced a significant decrease in the glomerular filtration rate but also presented a markedly increased incidence of mild eGFR reduction compared with the other groups. Moreover, within the groups with uric acid changes within 0.00–0.99 mg/dL and 1.00–1.99 mg/dL, in comparison with the group with negative uric acid changes, there was a notable elevation in the degree of glomerular filtration rate decline and the occurrence of mild eGFR reduction.

This study further categorized eGFR changes into five groups. The results indicated that the differences in SUA levels between baseline and follow-up were not statistically significant across the groups ($P>0.05$). However, since this study did not examine changes in prescriptions during the observation period, we cannot rule out the possibility of using antihyperuricemic medications during the study. A decrease in the follow-up eGFR to within 60–90 $ml{\cdot}min^{-1}{\cdot}(1.73\ m^2)^{-1}$ was used as the endpoint event, and after adjusting for other potential confounding factors, including age, sex, blood pressure, BMI, lipid levels, and blood glucose, the degree of change in uric acid remained a risk factor independently predicting mild eGFR reduction (OR value 1.347, $P<0.001$). Our results underscore that the extent of uric acid changes should be considered when assessing and managing kidney health, especially for individuals undergoing health examinations. Elevated uric acid levels can increase monocyte chemoattractant protein-1 expression, initiating an inflammatory response, which represents a fundamental mechanism leading to renal damage [21]. Additionally, increased uric acid levels can decrease the quantity of E-cadherin and promote the expression of α-smooth muscle actin, inducing epithelial–mesenchymal transition within the renal tubular epithelium and resulting in harm to the renal tubules [5, 22, 23]. A reduction in blood uric acid levels can mitigate oxidative stress while reducing renin–angiotensin–aldosterone system activation, consequently mitigating kidney damage [14, 24, 25]. Hyperuricemia can impair endothelial function in the kidneys through dual effects involving the upregulation of transforming growth factor-β1 via the Janus kinase/signal transducer and activator of transcription 3 pathways and a reduction in nitric oxide [5, 26]. Elevated uric acid levels can also lead to insulin resistance, alterations in adipokine secretion, and hypoadiponectinemia, which increase renal uric acid reabsorption. Microvascular dysfunction can further reduce uric acid excretion, exacerbating hyperuricemia [4, 27]. This goal can be achieved through the use of urate-lowering agents, which not only lower uric acid levels but also reduce the production of inflammatory factors and improve endothelial function, strengthening the protective effects on the kidneys [28, 29]. Importantly, however, this study did not consider the influence of urate-lowering medications.

The relationship between hyperuricemia and a decrease in the GFR is indeed complex, and the ability of the current study, which is retrospective in nature, to elucidate the underlying mechanisms is limited. The limitations of this study primarily manifest in two aspects. First, the assessment of uric acid changes relies on the difference between two time points over 3 years. This method may not fully capture the actual fluctuations in uric acid levels and their potential impact on accurately evaluating renal function. The current study only reflects data fluctuations without fully portraying the true extent of uric acid and renal function fluctuations. Second, the study utilized the eGFR as a renal function indicator rather than the more precise inulin clearance rate. Nevertheless, given that the study aimed to investigate longitudinal alterations in uric acid with eGFR, the use of the eGFR formula is unlikely to significantly affect the overall results. However, owing to these limitations, the findings of this study cannot be generalized to establish a conclusive relationship between blood uric acid levels and the GFR for all participants. However, further prospective cohort studies should be conducted to shed more light on the intricate relationships among these factors.

In conclusion, baseline blood uric acid levels alone cannot be used to determine renal function. Findings from our study suggest that, among individuals with normal baseline glomerular filtration rates, a slight elevation in blood uric acid levels is related to a minor decrease in the eGFR. Additionally, the degree of uric acid elevation correlates with the extent of the decrease in the eGFR. This underscores the importance of identifying and screening

for early risk factors for mild eGFR decline and determining the appropriate timing and interventions, especially in terms of lifestyle modifications. Diligent monitoring of alterations in uric acid and the glomerular filtration rate during regular health assessments can offer early indications of chronic kidney disease, potentially lowering the occurrence of mild eGFR decline and chronic kidney disease.

Abbreviations

CI	Confidence Intervals
CKD	Chronic Kidney Disease
CRP	C-Reactive Protein Serum
SUA	Uric Acid
HUA	Hyperuricemia
eGFR	estimate the Glomerular Filtration Rate
BMI	Body Mass Index
HDL	High-Density Lipoprotein Cholesterol
CKD-EPI	Chronic Kidney Disease Epidemiology Collaborative
LDL	Low-Density Lipoprotein Cholesterol
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ANOVA	Analysis of Variance

Acknowledgements
Not applicable.

Author contributions
NL participated in conceived of the study, and draft the manuscript and performed the statistical analysis and Collecting information and entering data and participated in follow-up visits. JW participated in Collecting information and entering data. JC participated in Responsible for follow-up visits. YC participated in the design of the study and conceived of the study. YT helped to draft the manuscript. XY participated in its design and coordination. All authors read and approved the final manuscript.

Funding
This study was assisted by the Xinjiang Medical University Educational Research and Teaching Reform Province (No. YG2021081), and supported by the 2023 Youth Research Start-up Special Fund Project (No. 2023YFY-QKQN-48).

Data availability
The data presented in this study are available on request from the corresponding author.

Declarations

Ethics approval and informed consent
This study was a retrospective study without any intervention measures. According to the Declaration of Helsinki, informed consent could not be signed. The Medical Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University approved the application form for exemption of informed consent (Ethics Approval No: K202303–08).

Consent for publication
A written informed consent was obtained from participants to publish this paper.

Competing interests
The authors declare no competing interests.

Received: 19 February 2024 / Accepted: 9 October 2024
Published online: 17 October 2024

References

1. Grams ME, Coresh J, Matsushita K, Ballew SH, Sang Y, Surapaneni A, et al. Estimated glomerular filtration rate, Albuminuria, and adverse outcomes: an individual-participant data Meta-Analysis. JAMA. 2023;330(13):1266–77. https://doi.org/10.1001/jama.2023.17002.
2. Shlipak MG, Tummalapalli SL, Boulware LE, Grams ME, Ix JH, Jha V, et al. The case for early identification and intervention of chronic kidney disease: conclusions from a kidney disease: improving global outcomes (KDIGO) Controversies Conference. Kidney Int. 2021;99(1):34–47. https://doi.org/10.1016/j.kint.2020.10.012.
3. Rossing P, Caramori ML, Chan JCN, Heerspink HJL, Hurst C, Khunti K, et al. Executive summary of the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in chronic kidney disease: an update based on rapidly emerging new evidence. Kidney Int. 2022;102(5):990–9. https://doi.org/10.1016/j.kint.2022.06.013.
4. Copur S, Demiray A, Kanbay M. Uric acid in metabolic syndrome: does uric acid have a definitive role? Eur J Intern Med. 2022;103:4–12. https://doi.org/10.1016/j.ejim.2022.04.022.
5. Gherghina ME, Peride I, Tiglis M, Neagu TP, Niculae A, Checherita IA. Uric acid and oxidative stress-relationship with Cardiovascular, metabolic, and renal impairment. Int J Mol Sci. 2022;23(6):3188. https://doi.org/10.3390/ijms23063188.
6. Kohagura K, Satoh A, Kochi M, Nakamura T, Zamami R, Tana T, et al. Urate-lowering drugs for chronic kidney disease with asymptomatic hyperuricemia and hypertension: a randomized trial. J Hypertens. 2023;41(9):1420–8. https://doi.org/10.1097/hjh.0000000000003484.
7. Yanai H, Adachi H, Hakoshima M, Katsuyama H. Molecular Biological and Clinical understanding of the pathophysiology and treatments of Hyperuricemia and its Association with Metabolic Syndrome, Cardiovascular diseases and chronic kidney disease. Int J Mol Sci. 2021;22(17):9221. https://doi.org/10.3390/ijms22179221.
8. Zhang M, Zhu X, Wu J, Huang Z, Zhao Z, Zhang X, et al. Prevalence of Hyperuricemia among Chinese adults: findings from two nationally Representative cross-sectional surveys in 2015-16 and 2018-19. Front Immunol. 2021;12:791983. https://doi.org/10.3389/fimmu.2021.791983.
9. Kawamoto R, Kikuchi A, Akase T, Ninomiya D, Tokumoto Y, Kumagi T. Alcohol consumption and serum uric acid are synergistically associated with renal dysfunction among community-dwelling persons. J Clin Lab Anal. 2021;35(6):e23812. https://doi.org/10.1002/jcla.23812.
10. Kawasoe S, Kubozono T, Salim AA, Ojima S, Yamaguchi S, Ikeda Y et al. J-shaped association between serum uric acid levels and the prevalence of a reduced kidney function: a cross-sectional study using Japanese Health Examination Data. Intern Med. 2023. https://doi.org/10.2169/internalmedicine.2474-23
11. Li N, Yang X, Wu J, Wang Y, Wang Z, Mu H. Correlation between the increase in serum uric acid and the rapid decline in kidney function in adults with normal kidney function: a retrospective study in Urumqi. China BMC Nephrol. 2023;24(1):103. https://doi.org/10.1186/s12882-023-03151-z.
12. Hu W, Wu XJ, Ni YJ, Hao HR, Yu WN, Zhou HW. Metabolic syndrome is independently associated with a mildly reduced estimated glomerular filtration rate: a cross-sectional study. BMC Nephrol. 2017;18(1):192. https://doi.org/10.1186/s12882-017-0597-3.
13. Chen-Xu M, Yokose C, Rai SK, Pillinger MH, Choi HK. Contemporary prevalence of gout and Hyperuricemia in the United States and Decadal trends: the National Health and Nutrition Examination Survey, 2007–2016. Arthritis Rheumatol. 2019;71(6):991–9. https://doi.org/10.1002/art.40807.
14. Bardin T, Magnat E, Clerson P, Richette P, Rouchon B. Epidemiology of gout and hyperuricemia in New Caledonia. Joint Bone Spine. 2022;89(2):105286. https://doi.org/10.1016/j.jbspin.2021.105286.
15. Liu X, Wang Y, Wang C, Shi C, Cheng C, Chen J, et al. A new equation to estimate glomerular filtration rate in Chinese elderly population. PLoS ONE. 2013;8(11):e79675. https://doi.org/10.1371/journal.pone.0079675.
16. Iseki K, Ikemiya Y, Inoue T, Iseki C, Kinjo K, Takishita S. Significance of hyperuricemia as a risk factor for developing ESRD in a screened cohort. Am J Kidney Dis. 2004;44(4):642–50.
17. Wingrove CS, Walton C, Stevenson JC. The effect of menopause on serum uric acid levels in non-obese healthy women. Metabolism. 1998;47(4):435–8. https://doi.org/10.1016/s0026-0495(98)90056-7.
18. Le HT, Le TT, Tran NMT, Nguyen TTT, Minh NCS, Le QT, et al. Serum uric acid levels and risk of Rapid decline of estimated glomerular filtration rate in patients with type 2 diabetes: findings from a 5-Year prospective

cohort study. Healthcare. (Basel). 2021;9(10):1341. https://doi.org/10.3390/healthcare9101341.
19. Liu P, Liang Y, Cui S, Hu K, Lin L, Shao X, et al. Association of uric acid with the decline in estimated glomerular filtration rate in middle-aged and elderly populations: evidence based on the China Health and Retirement Longitudinal Study. BMJ Open. 2023;13(5):e071771. https://doi.org/10.1136/bmjopen-2023-071771.
20. Tang X, Xu L, Meng RG, Du YQ, Liu SJ, Zhan SY, et al. Association between serum uric acid and the early marker of kidney function decline among Chinese middle-aged and older Population: evidence from the China Health and Retirement Longitudinal Study. Biomed Environ Sci. 2023;36(3):231–40. https://doi.org/10.3967/bes2023.026.
21. Yu S, Ren Q, Wu W. Effects of losartan on expression of monocyte chemoattractant protein-1 (MCP-1) in hyperuricemic nephropathy rats. J Recept Signal Transduct Res. 2015;35(5):458–61. https://doi.org/10.3109/10799893.2015.1006332.
22. Pintard C, Ben Khemis M, Liu D, Dang PM, Hurtado-Nedelec M, El-Benna J. Apocynin prevents GM-CSF-induced-ERK1/2 activation and -neutrophil survival independently of its inhibitory effect on the phagocyte NADPH oxidase NOX2. Biochem Pharmacol. 2020;177:113950. https://doi.org/10.1016/j.bcp.2020.113950.
23. Ho HJ, Shirakawa H. Oxidative stress and mitochondrial dysfunction in chronic kidney disease. Cells. 2022;12(1):88. https://doi.org/10.3390/cells12010088.
24. Filiopoulos V, Hadjiyannakos D, Vlassopoulos D. New insights into uric acid effects on the progression and prognosis of chronic kidney disease. Ren Fail. 2012;34(4):510–20. https://doi.org/10.3109/0886022x.2011.653753.
25. Piani F, Sasai F, Bjornstad P, Borghi C, Yoshimura A, Sanchez-Lozada LG, et al. Hyperuricemia and chronic kidney disease: to treat or not to treat. J Bras Nefrol. 2021;43(4):572–9. https://doi.org/10.1590/2175-8239-jbn-2020-u002.
26. Jung SW, Kim SM, Kim YG, Lee SH, Moon JY. Uric acid and inflammation in kidney disease. Am J Physiol Ren Physiol. 2020;318(6):F1327–40. https://doi.org/10.1152/ajprenal.00272.2019.
27. Kuwabara M, Fukuuchi T, Aoki Y, Mizuta E, Ouchi M, Kurajoh M, et al. Exploring the multifaceted Nexus of uric acid and health: a review of recent studies on Diverse diseases. Biomolecules. 2023;13(10):1519. https://doi.org/10.3390/biom13101519.
28. Kang DH, Nakagawa T, Feng L, Watanabe S, Han L, Mazzali M, et al. A role for uric acid in the progression of renal disease. J Am Soc Nephrol. 2002;13(12):2888–97. https://doi.org/10.1097/01.asn.0000034910.58454.fd.
29. Leoncini G, Barnini C, Manco L, Nobili G, Dotta D, Penso M, et al. Uric acid lowering for slowing CKD progression after the CKD-FIX trial: a solved question or still a dilemma? Clin Kidney J. 2022;15(9):1666–74. https://doi.org/10.1093/ckj/sfac075.

Publisher's note