Article

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Association of Decreased Kidney Function with Hyperuricemia in Different Subtypes of Prediabetes and Diabetes in Chinese Rural Residents: A Community-Based Cross-Sectional Study

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Background: We aimed to explore the risk factors and differences in decreased kidney function across the different subtypes of patients with prediabetes and diabetes among rural Chinese residents.

Methods: A total of 7581 residents of a community in Songjiang District, Shanghai, who were older than 40 years, were enrolled in this cross-sectional survey. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, and eGFR <60 mL/min/1.73 m^2 was defined as decreased kidney function. Subjects were divided into normal glucose tolerance (NGT), prediabetes, and diabetes groups according to a 75-g oral glucose tolerance test (OGTT) or self-reported diagnosis of diabetes.

Results: Of the 7581 subjects, 3578 had NGT, 1581 had diabetes and 2422 had prediabetes. In our study, 2.9% (47/1581) of diabetic patients and 2.4% (60/2422) of prediabetes patients in our study had decreased kidney function. The eGFR in the diabetes (94.1 $\pm$ 14.4 mL/min/1.73 m^2), combined glucose intolerance (CGI) (94.1 $\pm$ 13 mL/min/1.73 m^2) and impaired glucose tolerance (IGT) (93.1 $\pm$ 13.7 mL/min/1.73 m^2) groups was significantly lower than that in the NGT (95.7 $\pm$ 12.3 mL/min/1.73 m^2) and impaired fasting glucose (IFG) (95.6 $\pm$ 12.4 mL/min/1.73 m^2) groups ($p < 0.001$). Older age, age $\geq$60 years, female sex, and higher uric acid (UA) levels were common risk factors for decreased kidney function in the prediabetes and diabetes groups. Elevated levels of high-density lipoprotein cholesterol (HDL-C) were identified as a risk factor, while body mass index (BMI) $\geq$24 kg/m^2 was a protective factor against decreased kidney function in the prediabetes group. The area under the receiver operating characteristic (ROC) curve (AUC) of UA for predicting decreased kidney function was 0.7935 (95% Confidence interval (CI) 0.7058, 0.8329) in patients with diabetes and 0.7694 (95% CI 0.7058, 0.8329) in patients with prediabetes.

Conclusions: The prevalence of decreased kidney function in patients with different abnormal glycemic statuses was similar, whereas there were significant differences in eGFR levels among the different subtypes of prediabetes and diabetes. Older age, age $\geq$60 years, female sex, and hyperuricemia were common risk factors for decreased kidney function in prediabetes and diabetes patients. Reducing UA levels in prediabetes and diabetes patients may protect kidney function among rural Chinese residents.

Keywords: uric acid; Chronic Kidney Disease; prediabetes; diabetes

Introduction

The high prevalence of Chronic Kidney Disease (CKD) is associated with high mortality rates. CKD poses a substantial public health burden [1]. CKD is defined as a persistent abnormality in kidney structure or function, indicated by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 or albuminuria of 30 mg per 24 hours for 3 months [2]. In China, the overall prevalence of Chronic Kidney Disease was recorded at 10.8%. Risk factors for CKD include age, sex, hypertension, diabetes, history of cardiovascular disease, hyperuricemia, area of residence, and economic status [3].

Renal function and glucose metabolism interact closely with each other. In China, CKD and end-stage kidney disease are primarily caused by diabetes, which is

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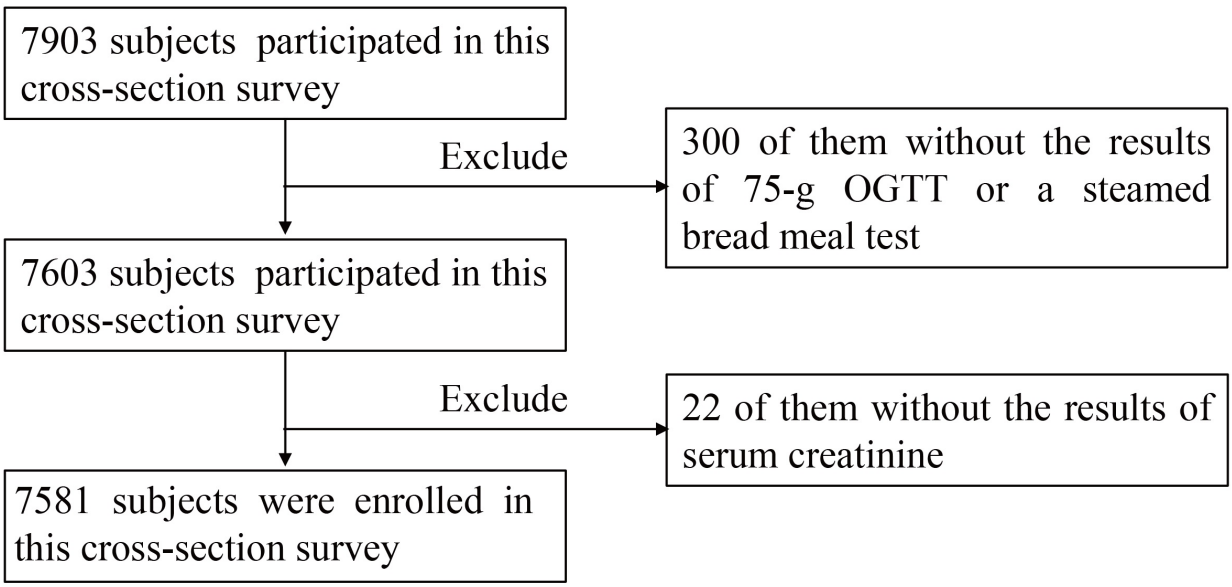

Fig. 1. Flow chart of the study subjects. OGTT, oral glucose tolerance test.

the leading contributing factor [4,5]. Prediabetes is also associated with the progression of CKD [6,7]. Furthermore, chronic renal insufficiency can lead to abnormal glucose and insulin metabolism [8]. A GFR of less than 60 mL/min/1.73 m^2 (half the normal value in young adults, which is approximately 125 mL/min/1.73 m^2) is considered a decline in kidney function and is linked to an increased risk of complications related to CKD [9]. Several studies have investigated the prevalence of decreased kidney function and associated risk factors in the general population and among those with diabetes [3,4,10–12]. However, limited research has been conducted on the risk factors associated with decreased kidney function based on abnormal glycemic status.

The objective of this study was to explore the risk factors for and differences in decreased kidney function among individuals with different glycemic statuses, including prediabetes and diabetes.

Methods

Study Population

A total of 7903 residents aged over 40 years from a community in Songjiang District, Shanghai, were enrolled in this cross-sectional survey. Three hundred participants were excluded due to missing results of a 75-g oral glucose tolerance test (OGTT) or a steamed bread meal test. Twenty-two patients were excluded because they did not have serum creatinine levels. Ultimately, 7581 participants were included in this study (Fig. 1). No patients had hypothyroidism, hyperthyroidism, or chronic renal failure. The study was approved by the ethics committee of Shanghai Jiao Tong University School of Medicine affiliated with Shanghai General Hospital (2013KY083).

Data Collection

All subjects underwent standardized interviews, including the completion of a detailed questionnaire (**Supplementary File 1**) and assessment of anthropometric indices and smoking and alcohol consumption statuses by trained research staff.

Physical examinations were performed in the fasting state. Blood pressure was measured three consecutive times and the average of these three measurements was documented for all subjects. Height, weight, waist circumference (WC), and hip circumference (HC) were measured with the subjects standing. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m), and the waist-to-hip ratio (WHR) was calculated as WC (cm) divided by HC (cm). Fat mass (kg), muscle mass (kg), Fat percentage, and Fat/muscle ratio were estimated by body impedance analysis (Tanita BC-420 MA; Tanita, Shanghai, China).

Subjects without diabetes underwent a 75-g OGTT, and subjects with diabetes underwent a steamed bread meal test after an overnight fast of over 10 hours. Serum glucose, creatinine (Cr), uric acid (UA), insulin, total cholesterol (TCH), triglyceride (TGs), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels were measured enzymatically using an automatic biochemistry analyzer. Hemoglobin A1C (HbA1c) was measured using a high-performance liquid chromatography method. All tests are completed in the same lab within a day after blood collection.

Insulin resistance and β-cell function were estimated using a homeostasis model assessment (HOMA) index. HOMA-IR was defined as [Fasting insulin (μU/mL) × fasting glucose (mmol/L)]/22.5. HOMA-β was defined as [20

× Fasting insulin (μU/mL)]/[fasting glucose (mmol/L) – 3.5] [13]. Based on the average value of HOMA-β in our study, better insulin secretion capacity was defined as HOMA-β >71.7. Insulin resistance was defined as HOMA-IR ≥2.8. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to calculate the estimated glomerular filtration rate (eGFR), and eGFR <60 mL/min/1.73 m^2 was defined as decreased kidney function [9].

Diagnostic Criteria and Definition

The diagnostic criteria for diabetes and prediabetes were established according to the guidelines set by the World Health Organization (WHO) [14]. The subjects were divided into different groups according to the results of the OGTT: normal glucose tolerance (NGT) [fasting blood glucose (FBG) <6.1 mmol/L and 2h postprandial glucose (2hPG) (75-g glucosepost) <7.8 mmol/L], prediabetes [including impaired fasting glucose (IFG): 6.1 ≤ FBG < 7.0 mmol/L and 2hPG <7.8 mmol/L; impaired glucose tolerance (IGT): FBG <6.1 mmol/L and 7.8 ≤ 2hPG < 11.1 mmol/L; combined glucose intolerance (CGI): 6.1 ≤ FBG < 7.0 mmol/L and 7.8 ≤ 2hPG < 11.1 mmol/L] and diabetes (FBG ≥7.0 mmol/L or/and 2hPG ≥11.1 mmol/L).

Hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure (DBP) ≥90 mmHg or treatment of previously diagnosed hypertension [15].

Hyperuricemia was defined as ≥420 μmol/L in males, UA ≥360 μmol/L in females or treatment of previously diagnosed hyperuricemia [16].

The criteria for defining metabolic syndrome were based on the guidelines provided by the International Diabetes Federation (IDF) [17,18]: Central obesity, which is defined as having a waist circumference of at least 90 cm for men or 80 cm for women in Asians [19]. In addition to central obesity, a person must have at least two of the following conditions: (1) Elevated triglyceride levels of 1.7 mmol/L or higher, or receiving treatment for this lipid abnormality; (2) Low levels of HDL-cholesterol, with levels below 1.03 mmol/L in men and below 1.29 mmol/L in women, or receiving treatment for this lipid abnormality; (3) High blood pressure, with systolic blood pressure of 130 mmHg or higher and diastolic blood pressure of 85 mmHg or higher, or receiving treatment for previously diagnosed hypertension; and (4) Elevated fasting plasma glucose levels of 5.6 mmol/L or higher, or previously diagnosed with type 2 diabetes [17].

Statistical Analysis

Statistics Analysis System (SAS) software (version 9.4; SAS Institute Inc., Cary, NC, USA) was used to analyze the data. An independent-samples *t*-test or one-way ANOVA was used to analyze continuous data. Data are presented as mean ± standard deviation (SD). The chi-square test was used to analyze categorical variables. Unconditional logistic regression models were used to calculate Odds ratios (ORs) and 95% Confidence intervals (CIs) for the variables. The Student-Newman-Keuls (SNK) test was used for multiple comparisons. A receiver operating characteristic (ROC) curve was plotted to establish a logistic regression model for the eGFR decline in patients with prediabetes and diabetes. Statistical significance was set at $p < 0.05$.

Results

A total of 7581 participants, all aged 40 years or older, were included in this study. Table 1 presents the clinical characteristics of the subjects, stratified by different abnormal glycemic statuses based on the 75-g OGTT results or self-reported previously diagnosed diabetes. Of the 7581 participants, 3578 had NGT, 1581 had diabetes, and 2422 had prediabetes (538 had IFG, 1344 had IGT, and 540 had CGI). An overall significant difference was found among the five groups in terms of age, sex, smoking, alcohol consumption, BMI, waist circumference, waist-hip ratio, Fat mass, blood pressure, UA, glucometabolic level, HOMA-IR, HOMA-β, lipid profiles, and eGFR. The eGFR in the diabetes (94.1 ± 14.4 mL/min/1.73 m^2), CGI (94.1 ± 13 mL/min/1.73 m^2) and IGT (93.1 ± 13.7 mL/min/1.73 m^2) groups was significantly lower than that in the NGT (95.7 ± 12.3 mL/min/1.73 m^2) and IFG (95.6 ± 12.4 mL/min/1.73 m^2) groups ($p < 0.001$). There was no significant difference in eGFR between the NGT and IFG groups, and no significant difference in eGFR among the diabetes, CGI, and IGT groups (Table 1).

Sixty of the 2422 prediabetes patients had an eGFR <60 mL/min/1.73 m^2 in this study. The age, proportion of females, prevalence of BMI ≥24 kg/m^2, UA level, prevalence of hypertension, and prevalence of hyperuricemia were higher and DBP was lower in prediabetes patients with eGFR <60 mL/min/1.73 m^2. After adjusting for sex, age, smoking, alcohol consumption, BMI and UA, age [OR 1.176, 95% CI (1.135, 1.219)], age ≥60 years [OR 17.723, 95% CI (5.397, 58.200)], HDL [OR 2.607, 95% CI (1.108, 6.138)], UA [OR 1.012, 95% CI (1.009, 1.016)] and hyperuricemia [OR 7.794, 95% CI (4.090, 14.853)] were risk factors for eGFR <60 mL/min/1.73 m^2 among patients with prediabetes. Male [OR 0.393, 95% CI (0.187, 0.829)] and BMI ≥24 kg/m^2 [OR 0.526, 95% CI (0.277, 0.998)] were protective factors against an eGFR <60 mL/min/1.73 m^2 among patients with prediabetes (Table 2).

Forty-seven of the 1581 diabetes patients had an eGFR <60 mL/min/1.73 m^2 in this study. Age, proportion of females, SBP, UA level, prevalence of HOMA-β >71.7, prevalence of hypertension, and prevalence of hyperuricemia were higher, while DBP was lower in diabetes patients with eGFR <60 mL/min/1.73 m^2. After adjusting for sex, age, smoking, alcohol consumption, BMI

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Table 1. Characteristics of the subjects stratified by glycemic status.

	NGT	Prediabetes			Diabetes		
		IFG	IGT	CGI		χ^2/F	*p*
N	3578	538	1344	540	1581		
Age (years)	58.7 ± 9.2	59.7 ± 9.1	61.6 ± 10	61.6 ± 9.5	62.5 ± 9.7	58.12	<0.001
<55, N (%)	1391 (38.9)	178 (33.1)	375 (27.9)	136 (25.2)	369 (23.3)	201.75	<0.001
55–64, N (%)	1378 (38.5)	219 (40.7)	519 (38.6)	235 (43.5)	634 (40.1)		
≥65, N (%)	809 (22.6)	141 (26.2)	450 (33.5)	169 (31.3)	578 (36.6)		
Sex, N (%)						46.04	<0.001
Female	1955 (54.6)	237 (44.1)	794 (59.1)	315 (58.3)	805 (50.9)		
Male	1623 (45.4)	301 (55.9)	550 (40.9)	225 (41.7)	776 (49.1)		
Smoking, N (%)						29.89	<0.001
No	2510 (72.3)	365 (70.6)	1030 (78.4)	409 (79.3)	1151 (74.7)		
Yes	964 (27.7)	152 (29.4)	283 (21.6)	107 (20.7)	390 (25.3)		
Alcohol consumption, N (%)						22.52	<0.001
No	2964 (85.9)	403 (78.7)	1116 (86)	431 (83)	1277 (83.6)		
Yes	485 (14.1)	109 (21.3)	182 (14)	88 (17)	251 (16.4)		
BMI (kg/m^2)	23.7 ± 3.1	24.8 ± 3.5	24.7 ± 3.4	25.4 ± 3.4	25.6 ± 3.5	112.16	<0.001
<24, N (%)	1985 (56.8)	213 (40.7)	542 (41.1)	172 (32.6)	490 (31.8)	346.41	<0.001
≥24, N (%)	1509 (43.2)	310 (59.3)	776 (58.9)	355 (67.4)	1052 (68.2)		
Waist-hip ratio, N (%)						143.80	<0.001
Female <0.85 male <0.9	1448 (40.5)	172 (32.0)	410 (30.5)	144 (26.7)	397 (25.1)		
Female ≥0.85 male ≥0.9	2130 (59.5)	366 (68.0)	934 (69.5)	396 (73.3)	1184 (74.9)		
WC (cm), N (%)						297.40	<0.001
Female <80 male <90	2191 (63.5)	245 (49.2)	635 (48.7)	204 (39.6)	618 (40.6)		
Female ≥80 male ≥90	1258 (36.5)	253 (50.8)	670 (51.3)	311 (60.4)	905 (59.4)		
SBP (mmHg)	131.6 ± 16.8	138.7 ± 16.1	137.4 ± 17.2	141.4 ± 18	144.4 ± 18.8	162.88	<0.001
DBP (mmHg)	76.4 ± 9.7	79.9 ± 9.4	78.1 ± 10	79.1 ± 10.6	79.1 ± 10.0	31.38	<0.001
FBG (mmol/L)	5.4 ± 0.4	6.3 ± 0.2	5.5 ± 0.4	6.4 ± 0.2	7.8 ± 2.4	1384.13	<0.001
PBG (mmol/L)	6.1 ± 1.1	6.3 ± 1.0	8.9 ± 0.9	9.2 ± 0.9	14.7 ± 5.0	3603.37	<0.001
HbA1c (%)	5.4 ± 0.3	5.6 ± 0.4	5.6 ± 0.4	5.8 ± 0.4	6.8 ± 1.4	980.03	<0.001
FINS (μU/mL)	6.6 ± 3.5	8.7 ± 4.6	8.2 ± 4.5	9.9 ± 5.4	10.5 ± 6.9	202.76	<0.001
UA (μmol/L)	306.1 ± 79.7	328.3 ± 85.3	329.2 ± 88.8	333.3 ± 83.4	329.6 ± 87.3	38.23	<0.001
TCH (mmol/L)	5.0 ± 0.9	5.2 ± 0.9	5.2 ± 0.9	5.4 ± 1	5.3 ± 1	25.05	<0.001
TGs (mmol/L)	1.4 ± 1.0	1.7 ± 1.3	1.8 ± 1.4	2.1 ± 2.5	2 ± 1.8	63.44	<0.001
HDL (mmol/L)	1.6 ± 0.4	1.6 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	15.08	<0.001
LDL (mmol/L)	2.8 ± 0.7	2.9 ± 0.8	2.9 ± 0.8	3.1 ± 0.8	3 ± 0.8	21.63	<0.001
HOMA-IR	1.6 ± 0.9	2.5 ± 1.3	2 ± 1.1	2.8 ± 1.5	3.7 ± 2.8	485.86	<0.001
<2.8, N (%)	3257 (91)	368 (68.4)	1077 (80.2)	313 (58)	743 (47.6)	1263.96	<0.001
≥2.8, N (%)	321 (9)	170 (31.6)	266 (19.8)	227 (42)	817 (52.4)		
HOMA-β	70 ± 33.7	61 ± 31.1	78.2 ± 38.7	66.6 ± 34.1	55 ± 37.0	87.58	<0.001
eGFR (mL/min/1.73 m^2)	95.7 ± 12.3	95.6 ± 12.4	93.1 ± 13.7^{a,b}	94.1 ± 13^{a,b}	94.1 ± 14.4^{a,b}	11.66	<0.001
Fat (kg)	17.6 ± 16.4	18.7 ± 8.7	19 ± 10.0	20.3 ± 10.8	20 ± 8.2	11.54	<0.001
Fat%	27.5 ± 8	28.4 ± 8.1	29.8 ± 8.5	30.8 ± 8	30.2 ± 8.7	44.97	<0.001
Muscle (kg)	41.9 ± 15.8	43.5 ± 8.6	41 ± 7.8	42.3 ± 19.4	43.2 ± 15.1	5.66	<0.001
Fat/Muscle	2.9 ± 2.1	2.8 ± 1.5	2.7 ± 2.4	2.4 ± 1.8	2.7 ± 3.5	6.46	<0.001
Hypertension, N (%)						547.27	<0.001
No	2128 (60.3)	221 (41.8)	587 (44.3)	183 (34.3)	421 (26.9)		
Yes	1402 (39.7)	308 (58.2)	739 (55.7)	350 (65.7)	1144 (73.1)		
Metabolic syndrome, N (%)						875.94	<0.001
No	2768 (80.3)	253 (50.9)	814 (62.5)	218 (42.4)	632 (41.6)		
Yes	678 (19.7)	244 (49.1)	489 (37.5)	296 (57.6)	888 (58.4)		

Table 1. Continued.

	NGT	Prediabetes			Diabetes		
		IFG	IGT	CGI		χ^2/F	*p*
Hyperuricemia, N (%)						64.03	<0.001
No	3259 (91.1)	464 (86.2)	1140 (84.8)	448 (83)	1365 (86.3)		
Yes	319 (8.9)	74 (13.8)	204 (15.2)	92 (17)	216 (13.7)		

[a] Compared with NGT $p < 0.05$, [b] Compared with IFG $p < 0.05$. NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; CGI, combined glucose intolerance; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; UA, uric acid; TCH, total cholesterol; TGs, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HOMA, homeostasis model assessment; eGFR, estimated glomerular filtration rate; WC, waist circumference; HbA1c, Hemoglobin A1C; FINS, Fasting insulin; PBG, Postprandial blood glucose.

and UA, age [OR 1.156, 95% CI (1.109, 1.205)], age ≥60 years [OR 9.4311, 95% CI (2.686, 33.116)], UA [OR 1.012, 95% CI (1.009, 1.016)] and hyperuricemia [OR 10.442, 95% CI (5.087, 21.434)] were risk factors for eGFR <60 mL/min/1.73 m^2 in individuals with prediabetes. Male [OR 0.289, 95% CI (0.116, 0.724)] was a protective factor against an eGFR <60 mL/min/1.73 m^2 among individuals with diabetes (Table 3).

ROC curve was created to assess and compare UA, FBG, 2hPG, HbA1c, HOMA-β and their combinations for the prediction of the decline in eGFR in prediabetes and diabetes patients. In prediabetes patients, the areas under the ROC curve (AUC) of UA, FBG, 2hPG, HbA1c and HOMA-β for the decline in eGFR were 0.7694 (95% CI 0.7058, 0.8329, $p < 0.001$), 0.5403 (95% CI 0.4608, 0.6199, $p = 0.29$), 0.5840 (95% CI 0.5094, 0.6587, $p = 0.03$), 0.5400 (95% CI 0.4566, 0.6234, $p = 0.29$) and 0.5319 (95% CI 0.4633, 0.6004, $p = 0.40$), respectively. The combined AUC of these factors was 0.7784 (95% CI 0.7139, 0.8428). In diabetes patients, the AUC of UA, FBG, 2hPG, HbA1c and HOMA-β for the decline in eGFR were 0.7935 (95% CI 0.7325, 0.8545, $p < 0.001$), 0.5564 (95% CI 0.4584, 0.6545, $p = 0.21$), 0.5162 (95% CI 0.4346, 0.5978, $p = 0.72$), 0.4938 (95% CI 0.3986, 0.5889, $p = 0.89$) and 0.5627 (95% CI 0.4699, 0.6554, $p = 0.17$), respectively. The combined AUC for these factors was 0.8001 (95% CI 0.7417, 0.8584) (Fig. 2, Table 4).

Discussion

In this community-based cross-sectional study, 52.8% of the subjects over 40 years of age had abnormal glucose metabolism. The prevalence of diabetes and prediabetes was 20.9% and 31.9%, respectively, according to the World Health Organization (WHO) diagnostic criteria. According to a national cross-sectional study of a Chinese population, the prevalence of diabetes and prediabetes in individuals aged 40–59 years was 15.8% and 42.9%, respectively, according to the American Diabetes Association (ADA) diagnostic criteria [20]. Moreover, the prevalence of diabetes and prediabetes in individuals aged >60 years is 30.2% and 47.7%, respectively [20]. The prevalence of prediabetes in our study was lower than that reported in a previous study, which may be due to the lower FBG cutoff level for prediabetes in the ADA diagnostic criteria.

Most previous studies have focused on the prevalence of decreased renal function in the general population. In a national sample of Chinese adults, the prevalence of reduced kidney function was 1.7% [3]. Few studies have examined the prevalence of reduced kidney function in individuals with different abnormal glycemic statuses. Duan *et al*. [21] reported that the prevalence of decreased kidney function in patients with diabetes was 4.6% in a sample of rural Chinese residents. In adults with both hypertension and diabetes, the prevalence can reach 7.3% [22]. In our study, 2.9% (47/1581) of rural Chinese residents with diabetes had decreased kidney function. This prevalence is lower than that reported in a previous study. Due to differences in age groups, geographic regions, and methods of eGFR assessment, the prevalence of reduced kidney function varies widely. Community-based studies have shown that the prevalence of decreased kidney function is 16.4% in the population aged >65 years [23], and only 5.4% in the population aged >18 years [24] in Shanghai. In our study, the average age of prediabetes and diabetes patients was approximately 60 years, and the younger age of the subjects may be one of the factors that caused the low prevalence of decreased kidney function. Furthermore, the participants in our study were from Songjiang District, an undeveloped district in Shanghai. The prevalence of decreased kidney function in developed countries was considerably higher than that in developing countries [12,25,26]. Participants from underdeveloped districts in this study may have also been affected by the low prevalence of decreased kidney function.

Notably, similar to diabetes patients, 2.4% (60/2422) of the prediabetes patients in our study had decreased kidney function. The prevalence of decreased kidney function in prediabetes patients has not yet been independently assessed. Our findings indicate that differences in kidney function should also be a focus in different subtypes of prediabetes patients. There were significant differences

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Table 2. Risk factors for the decline in eGFR in prediabetes patients.

	eGFR ≥60 (N = 2362)	eGFR <60 (N = 60)	χ^2/t	p	Estimate	Standard Error	Wald Chi-Square	OR (95% CI)*
Sex, N (%)			0.92	0.336				
Female	1309 (55.4)	37 (61.7)						1
Male	1053 (44.6)	23 (38.3)			–0.93	0.38	6.02	0.393 (0.187, 0.829)
Age (years)	60.8 ± 9.4	76.9 ± 8.3	13.20	<0.001	0.16	0.03	80.74	1.176 (1.135, 1.219)
<60, N (%)	1209 (51.2)	3 (5.0)	49.93	<0.001				1
≥60, N (%)	1153 (48.8)	57 (95.0)			2.87	0.61	22.46	17.723 (5.397, 58.200)
Smoking, N (%)			2.70	0.1				
No	1755 (76.7)	49 (86)						1
Yes	534 (23.3)	8 (14)			0.16	0.53	0.09	1.177 (0.418, 3.311)
Alcohol consumption, N (%)			5.02	0.025				
No	1897 (83.5)	53 (94.6)						1
Yes	376 (16.5)	3 (5.4)			–0.99	0.73	1.86	0.370 (0.088, 1.546)
BMI (kg/m^2)	24.9 ± 3.4	24.7 ± 4.3	0.29	0.77	–0.01	0.04	0.11	0.986 (0.911, 1.069)
<24, N (%)	896 (38.8)	31 (51.7)	4.05	0.044				1
≥24, N (%)	1412 (61.2)	29 (48.3)			–0.64	0.33	3.86	0.526 (0.277, 0.998)
Waist-hip ratio, N (%)			0.73	0.394				
Female <0.85 male <0.9	711 (30.1)	15 (25)						1
Female ≥0.85 male ≥0.9	1651 (69.9)	45 (75)			0.004	0.36	0.0001	1.004 (0.491, 2.055)
WC (cm), N (%)			0.25	0.617				
Female <80 male <90	1055 (46.7)	29 (50)						1
Female ≥80 male ≥90	1205 (53.3)	29 (50)			–0.40	0.33	1.47	0.672 (0.354, 1.277)
SBP (mmHg)	138.5 ± 17.1	141.9 ± 22.2	1.19	0.24	–0.01	0.009	1.56	0.989 (0.972, 1.006)
DBP (mmHg)	78.8 ± 10	73.2 ± 11	4.30	<0.001	–0.03	0.02	3.17	0.970 (0.938, 1.003)
FBG (mmol/L)	5.9 ± 0.5	5.8 ± 0.6	1.41	0.159	–0.13	0.30	0.18	0.878 (0.483, 1.596)
PBG (mmol/L)	8.4 ± 1.4	8.7 ± 1.4	1.75	0.08	–0.0001	0.11	0	1.000 (0.803, 1.245)
HbA1c (%)	5.6 ± 0.4	5.7 ± 0.5	1.05	0.298	–0.20	0.38	0.29	0.818 (0.398, 1.682)
FINS (μU/mL)	8.7 ± 4.8	8.6 ± 4.4	0.11	0.91	–0.06	0.04	2.19	0.942 (0.871, 1.019)
UA (μmol/L)	327.4 ± 84.6	427.8 ± 112.9	6.84	<0.001	0.01	0.002	50.94	1.012 (1.009, 1.016)
TCH (mmol/L)	5.2 ± 0.9	5.3 ± 0.9	0.36	0.722	0.11	0.16	0.50	1.121 (0.818, 1.536)
TGs (mmol/L)	1.8 ± 1.7	1.9 ± 1.8	0.16	0.874	–0.02	0.11	0.02	0.985 (0.791, 1.227)
HDL (mmol/L)	1.5 ± 0.4	1.6 ± 0.4	0.35	0.724	0.96	0.44	4.81	2.607 (1.108, 6.138)
LDL (mmol/L)	3 ± 0.8	2.9 ± 0.8	0.05	0.962	–0.02	0.19	0.008	0.983 (0.671, 1.439)
HOMA-IR			0.18	0.675				
<2.8	1713 (72.6)	45 (75)						1
≥2.8	648 (27.4)	15 (25)			–0.44	0.37	1.44	0.639 (0.308, 1.329)
HOMA-β			0.49	0.486				
≤71.7	1348 (58.2)	37 (62.7)						1
>71.7	969 (41.8)	22 (37.3)			–0.58	0.37	2.53	0.557 (0.271, 1.146)
Fat%			0.04	0.845				
Female ≤30 or male ≤25	223 (17.4)	6 (16.2)						1
Female >30 or male >25	1055 (82.6)	31 (83.8)			0.37	0.61	0.36	1.444 (0.434, 4.807)
Muscle/Fat	2.6 ± 2.1	2.6 ± 1.3	0.39	0.698	0.05	0.09	0.24	1.047 (0.870, 1.260)
Hypertension, N (%)			8.37	0.004				
No	977 (42)	14 (23.3)						1
Yes	1351 (58)	46 (76.7)			0.06	0.37	0.03	1.063 (0.513, 2.202)
Metabolic syndrome, N (%)			0.56	0.455				
No	1250 (55.4)	35 (60.3)						1
Yes	1006 (44.6)	23 (39.7)			–0.45	0.37	1.50	0.635 (0.307, 1.312)
Hyperuricemia, N (%)			62.94	<0.001				
No	2023 (85.6)	29 (48.3)						1
Yes	339 (14.4)	31 (51.7)			2.05	0.33	38.95	7.794 (4.090, 14.853)

*Adjusted for sex, age, smoking status, alcohol consumption, BMI, and UA. OR, Odds ratio. CI, Confidence interval.

Table 3. Risk factors for the decline in eGFR in diabetes patients.

	eGFR ≥60 (N = 1534)	eGFR <60 (N = 47)	χ^2/t	p	Estimate	Standard Error	Wald Chi-Square	OR (95% CI)*
Sex, N (%)			1.45	0.228				
Female	777 (50.7)	28 (59.6)						1
Male	757 (49.3)	19 (40.4)			–1.24	0.47	7.03	0.289 (0.116, 0.724)
Age (years)	62.1 ± 9.4	75.6 ± 8.4	26.84	<0.001	0.14	0.02	45.03	1.156 (1.109, 1.205)
<60, N (%)	681 (44.4)	3 (6.4)		<0.001				1
≥60, N (%)	853 (55.6)	44 (93.6)			2.27	0.64	12.64	9.4311 (2.686, 33.116)
Smoking, N (%)			0.42	0.519				
No	1114 (74.6)	37 (78.7)						1
Yes	380 (25.4)	10 (21.3)			0.96	0.60	2.59	2.625 (0.811, 8.499)
Alcohol consumption, N (%)			3.39	0.066				
No	1234 (83.3)	43 (93.5)						1
Yes	248 (16.7)	3 (6.5)			–0.85	0.79	1.15	0.428 (0.091, 2.015)
DM duration (years)			2.18	0.14				
<5, N (%)	1242 (81.0)	34 (72.3)						
≥5, N (%)	292 (19.0)	13 (27.7)			0.34	0.54	0.40	1.404 (0.492, 4.007)
Use of hypoglycemic drugs, N (%)			1.10	0.294				
No	1057 (68.9)	29 (61.7)						1
Yes	477 (31.1)	18 (38.3)			–0.09	0.48	0.03	0.917 (0.359, 2.342)
BMI (kg/m^2)	25.6 ± 3.5	26.0 ± 3.6	0.71	0.477	0.04	0.05	0.69	1.041 (0.946, 1.147)
<24, N (%)	475 (31.8)	15 (32.6)	0.02	0.902				1
≥24, N (%)	1021 (68.2)	31 (67.4)			0.12	0.39	0.10	1.179 (0.548, 2.538)
Waist-hip ratio, N (%)			0.92	0.339				
Female <0.85 male <0.9	388 (25.3)	9 (19.1)						1
Female ≥0.85 male ≥0.9	1146 (74.7)	38 (80.9)			0.23	0.44	0.27	1.262 (0.528, 3.016)
WC (cm), N (%)			3.36	0.067				
Female <80 male <90	605 (41)	13 (27.7)						1
Female ≥80 male ≥90	871 (59)	34 (72.3)			0.33	0.40	0.69	1.394 (0.638, 3.047)
SBP (mmHg)	144.1 ± 18.8	152.2 ± 18.2	2.85	0.004	0.004	0.009	0.16	1.004 (0.986, 1.022)
DBP (mmHg)	79.2 ± 10	74.8 ± 10.2	2.91	0.004	0.002	0.02	0.02	1.003 (0.966, 1.042)
FBG (mmol/L)	7.8 ± 2.4	7.5 ± 2.3	0.99	0.324	0.10	0.08	1.59	1.136 (0.949, 1.313)
PBG (mmol/L)	14.8 ± 4.9	14 ± 5.1	0.97	0.334	0.001	0.04	0.0006	1.000 (0.916, 1.093)
HbA1c (%)	6.8 ± 1.4	6.7 ± 1.4	0.29	0.773	0.18	0.14	1.61	1.225 (0.923, 1.625)
FINS (μU/mL)	10.5 ± 6.9	11.7 ± 8.1	1.17	0.241	0.007	0.03	0.05	1.008 (0.952, 1.066)
UA (μmol/L)	326.3 ± 84.3	437.9 ± 112.6	6.73	<0.001	0.01	0.002	47.97	1.012 (1.009, 1.016)
TCH (mmol/L)	5.3 ± 1	5 ± 1	1.46	0.145	–0.14	0.18	0.60	0.865 (0.601, 1.245)
TGs (mmol/L)	2.0 ± 1.8	2.2 ± 1.9	0.59	0.555	–0.007	0.12	0.003	0.989 (0.779, 1.257)
HDL (mmol/L)	1.5 ± 0.4	1.4 ± 0.4	1.88	0.061	–0.62	0.52	1.46	0.552 (0.203, 1.502)
LDL (mmol/L)	3.0 ± 0.8	2.9 ± 0.8	1.03	0.304	–0.04	0.22	0.03	0.956 (0.614, 1.488)
HOMA-IR			0.22	0.635				
<2.8	720 (47.5)	23 (51.1)						1
≥2.8	795 (52.5)	22 (48.9)			0.09	0.44	0.04	1.094 (0.463, 2.586)
HOMA-β			6.26	0.012				
≤71.7	906 (60.8)	18 (41.9)						1
>71.7	584 (39.2)	25 (58.1)			0.20	0.41	0.23	1.2186 (0.547, 2.712)
Fat%			/	0.598				
Female ≤30 or male ≤25	112 (15)	5 (17.9)						1
Female >30 or male >25	634 (85)	23 (82.1)			–0.91	0.77	1.42	0.402 (0.089, 1.806)
Muscle/Fat	2.7 ± 3.5	3.1 ± 4.2	0.74	0.459	0.02	0.03	0.6	1.024 (0.969, 1.081)
Hypertension, N (%)			4.92	0.027				
No	415 (27.3)	6 (12.8)						1
Yes	1103 (72.7)	41 (87.2)			0.15	0.56	0.07	1.161 (0.388, 3.478)

Journal of
BIOLOGICAL REGULATORS
and Homeostatic Agents

Table 3. Continued.

	eGFR ≥60 (N = 1534)	eGFR <60 (N = 47)	χ^2/t	p	Estimate	Standard Error	Wald Chi-Square	OR (95% CI)*
Metabolic syndrome, N (%)			1.13	0.287				
No	616 (41.8)	16 (34)						1
Yes	857 (58.2)	31 (66)			0.01	0.47	0.0007	1.012 (0.400, 2.558)
Hyperuricemia, N (%)			57.44	<0.001				
No	1342 (87.5)	23 (48.9)						1
Yes	192 (12.5)	24 (51.1)			2.34	0.36	40.87	10.442 (5.087, 21.434)

* Adjusted for sex, age, smoking, alcohol consumption, BMI, and UA levels. CI, Confidence interval.

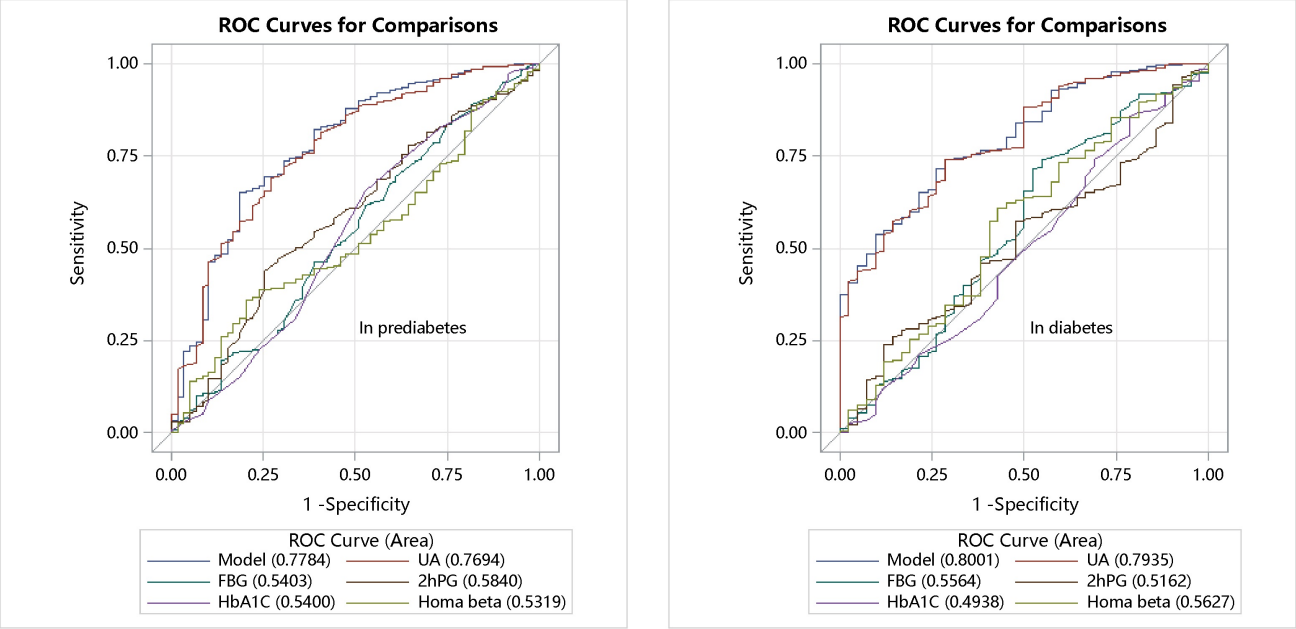

Fig. 2. Receiver operating characteristic (ROC) curve (AUC) of UA, FBG, 2h postprandial glucose (2hPG), HbA1c and HOMA-β as a predictive tool for the decline in eGFR in prediabetes and diabetes patients.

in eGFR levels between the different subtypes of prediabetes and diabetes. However, in the present study, we used the CKD-EPI equation to assess kidney function in patients with prediabetes and diabetes. Although this method is considered reliable in a wide population survey, it may not be accurate for specific populations, particularly patients with kidney insufficiency in China [27]. Additionally, proteinuria was not measured in this study. In the latest epidemiological survey in China, the prevalence of eGFR <60 mL/min/1.73 m^2 in the population was 2.2%, while the prevalence of proteinuria reached 6.7% [28]. Therefore, our study has certain limitations, and further research is required.

The risk factors for decreased kidney function were examined in prediabetes and diabetes patients in this study. The prediabetes and diabetes patients share many common risk factors, such as older age, age ≥60 years, female sex, UA level, and hyperuricemia. Older age has been widely reported as an independent factor associated with an increased risk of reduced kidney function in the general population and the population with diabetes [21,29,30]. With a rapidly developing economy, aging has become a major social problem in China [31]. We found that age ≥60 years increased the risk of decreased kidney function, with ORs of 17.723 (95% CI, 5.397–58.200) and 9.4311 (95% CI, 2.686–33.116) in prediabetes and diabetes patients, respectively. Sex differences were also observed in our study, and we found that females had a higher risk of decreased kidney function in the prediabetes and diabetes groups. The results are consistent with previous studies [32,33]. However, the mechanism underlying the sex disparity in decreased kidney function remains unclear. As age and sex are non-interventional factors, elderly females should receive more attention in terms of reducing interventional risk factors such as hyperuricemia to protect kidney function.

There was a notable association between obesity and a significantly increased risk of progression towards decreased kidney function. In addition to hemodynamic, structural, and histological renal changes, metabolic and biochemical alterations in overweight and obese patients

Table 4. The results of ROC and AUC of UA, FBG, 2hPG and HbA1c as a predictive tool for the decline in eGFR in prediabetes and diabetes patients.

	Prediabetes					Diabetes				
	Area	Standard Error	95% Wald Confidence Limits		*p*	Area	Standard Error	95% Wald Confidence Limits		*p*
UA	0.7694	0.0324	0.7058	0.8329	<0.001	0.7935	0.0311	0.7325	0.8545	<0.001
FBG	0.5403	0.0406	0.4608	0.6199	0.29	0.5564	0.0500	0.4584	0.6545	0.21
2hPG	0.5840	0.0381	0.5094	0.6587	0.03	0.5162	0.0416	0.4346	0.5978	0.72
HbA1c	0.5400	0.0426	0.4566	0.6234	0.29	0.4938	0.0485	0.3986	0.5889	0.89
HOMA-β	0.5319	0.0350	0.4633	0.6004	0.40	0.5627	0.0473	0.4699	0.6554	0.17

can lead to kidney disease [34]. Even overweight and obese patients without metabolic abnormalities exhibited an elevated risk for CKD progression [35,36]. However, some studies have reported that the association between BMI and CKD remains unclear. A meta-analysis showed that BMI was not significantly associated with CKD when evaluated as a continuous variable [37]. Vidar T N Stefansson *et al*. [38] also found that obesity measures (BMI, WC, and waist-to-hip ratio) were not risk factors for accelerated age-related GFR decline in the general population. In our study, we found that BMI was not significantly associated with decreased kidney function in diabetes patients and that BMI $\geq$24 kg/m^2 was a protective factor against decreased kidney function in prediabetes patients. We hypothesized that the differences in the results of various studies were due to the different pathophysiological changes caused by overweight and obesity in different sexes, age groups, races, and geographical regions.

We found that levels of UA and the presence of hyperuricemia have been identified as risk factors for decreased kidney function in individuals with prediabetes and diabetes. Urate-induced inflammasome activation affects kidney function via multiple pathways [39]. Previous studies have shown that hyperuricemia is associated with decreased kidney function in both the general and diabetic populations [21,24,40–42]. According to a prior community-based cohort study conducted on the Chinese population, it was observed that for each 1 mg/dL rise in UA from the baseline had an OR of 1.19 (95% CI, 1.04–1.38) for decreased kidney function [43]. Reducing the UA levels in prediabetes and diabetes patients would have a positively affects kidney function. However, it should be noted that dietary and lifestyle habits have a significant impact on uric acid and kidney function [44,45]. The participants in this study lived in the same community for a long time and we believe that there were no differences in their dietary habits. However, the effects of exercise habits on kidney function cannot be ignored. Previous studies have shown that regular moderate-intensity exercise has a protective effect on kidney function in the elderly [46]. In this study, we did not analyze the exercise and dietary habits of the subjects, which is one of the limitations of this study.

As common chronic diseases, hypertension, hyperglycemia, and dyslipidemia are considered risk factors for decreased kidney function in the general population [47, 48]. However, in our pressure and glucose levels were not associated with decreased kidney function in prediabetes and diabetes patients in our study. Moreover, we observed that elevated HDL levels were associated with an increased risk of decreased kidney function in individuals with prediabetes. Melsom *et al*. [49] also found that higher HDL levels were associated with accelerated GFR reduction in a general middle-aged non-diabetic population. It is generally believed that HDL is beneficial for healthy individuals, and a higher HDL level could reduce the risk of cardiovascular disease [50]. Further investigation is required to explore the correlation between HDL cholesterol levels and kidney function.

The ROC curve was used to compare the values of UA, FBG, 2hPG, HbA1c, HOMA-β and their combinations as predictors of decreased kidney function. We found that the AUCs of FBG, 2hPG, HbA1c, and HOMA-β were similar and had poor predictive abilities in prediabetes and diabetes patients. The AUCs of UA were 0.7694 (95% CI 0.7058, 0.8329) and 0.7935 (95% CI 0.7325, 0.8545) in prediabetes and diabetes patients, respectively, which showed good predictive ability. Therefore, we propose UA as a warning indicator of decreased kidney function in prediabetes and diabetes patients.

Our study has several limitations. First, due to some restrictions, albuminuria was not assessed in all samples. Second, as this was a community-based cross-sectional study, we did not follow up with the participants, and the level of evidence was not strong. Third, except for smoking and alcohol consumption, we did not evaluate lifestyle factors such as diet, sleep duration, and exercise habits, which may have affected the results. First, this was a cross-sectional observational study; therefore, causal inferences could not be drawn. To elucidate the causal relationships between uric acid levels, sex, age, and decreased kidney function in individuals with abnormal glucose metabolism, it is necessary to conduct large-scale multicenter prospective studies, as indicated by the current findings of this single-center cross-sectional study.

Journal of
BIOLOGICAL REGULATORS
and Homeostatic Agents

Conclusions

A total of 2.4% of the prediabetes patients and 2.9% of diabetes patients had decreased kidney function. Notable disparities were observed in eGFR levels among the various subtypes of prediabetes and diabetes. More attention should be paid to the assessment of renal function decline in patients with pre diabetes. Older age, age $\geq$60 years, female sex, UA levels, and hyperuricemia were common risk factors for decreased kidney function in prediabetes and diabetes patients. In particular, early in the course of different abnormal glycemic statuses, strengthening the reduction of UA levels in prediabetes and diabetes patients may protect kidney function.

Availability of Data and Materials

All data included in this study are available upon request by contacting the corresponding authors.

Author Contributions

YFW, YDP, XYD and YHM designed the research study. LM, CHL, XJW, NGF and XHW participated in epidemiological investigations, data organization, and formal analysis. JYJ analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read 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

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Shanghai Jiao Tong University School of Medicine affiliated with Shanghai General Hospital (2013KY083). All the participants provided written informed consent.

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Conflict of Interest

The authors declare no conflict of interest. Yuhang Ma is serving as one of the Editorial Board of this journal. We declare that Yuhang Ma had no involvement in the peer review of this article and has no access to information regarding its peer review. Junyi Jiang is an employee of Changsha Duxact Biotech Co., Ltd. This corporation had no role in the design of the study in the collection, analyses, or interpretation of data in the writing of the manuscript, or in the decision to publish the results.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.23812/j.biol.regul.homeost.agents.20243806.420.

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