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Estimation of the prevalence of type 2 diabetes in combination with diabetic kidney disease and identification of the associated factors in patients attending primary hospitals in Anhui Province, China

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Abstract

Objective: To evaluate the prevalence of type 2 diabetes mellitus (T2DM) with chronic kidney disease (DM-CKD) and identify the associated factors in patients attending primary hospitals in Anhui Province, China.

Methods: A multi-stage sampling method was used to collect the demographic information, general clinical data, and details of the kidney disease of patients in 2019 through a questionnaire survey, physical examination, and laboratory examination.

Results: A total of 1067 patients with T2DM were studied, of whom 345 had chronic kidney disease (CKD; 32.33%); 18.8%, 12.2%, 58.0%, 9.9% and 1.2% of the participants had stages 1 to 5 CKD. Fifty-point-three percent of the participants were female and they were 59 ± 11.3 years old. Multivariate regression analysis revealed that age, systolic blood pressure, the duration of diabetes, hyperlipidaemia, and smoking were associated with DM-CKD. The duration of diabetes was positively associated with body mass index, 2-hour postprandial glucose, fasting blood glucose concentration, glycosylated haemoglobin, total cholesterol concentration and triglyceride concentration.

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Conclusions: The incidence of DM-CKD is relatively high in primary hospitals in Anhui Province. Appropriate preventive and therapeutic measures should be instituted according to the age, the duration of diabetes, sex, hypertension, smoking habits, and lipidaemia of patients.

Keywords
Type 2 diabetes mellitus, chronic kidney disease, diabetes mellitus, systolic blood pressure, hyperlipidaemia, Anhui Province

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Introduction

Chronic kidney disease (CKD) is a clinical syndrome that is characterised by long-term abnormalities in renal structure or function and a progressive decline in glomerular filtration. If the underlying disease is not treated in a timely fashion, it eventually progresses to end-stage kidney disease (ESRD), which places a substantial healthcare burden on the patient and family, as well as an economic burden on the country. CKD can be categorised into five stages, according to the patient's estimated glomerular filtration rate (eGFR). Although the majority of patients with stages 1 to 3 CKD do not show a clinical manifestation of the disease, once clinical symptoms appear, the renal injury cannot be reversed. Instead, the early diagnosis of CKD and the introduction of appropriate treatments can significantly improve renal function and reduce the risk of mortality. The prevalence of CKD in adults in the US is now 11.3%, and worldwide, the prevalences of CKD stages 1 to 5 and 3 to 5 have been estimated to 13.4% and 10.6%, with 4.9 to 7.1 million patients with ESKD requiring kidney transplantation.[1,2] According to the 2018 US Renal Data System report, the prevalence of cardiovascular disease in patients of $\geq$66 years of age who have CKD is approximately twice as high as in those without.[3] Thus, the institution of early preventive measures and regular check-ups should significantly reduce the incidence of such complications.

Diabetes mellitus is a polygenic inherited metabolic disorder that is also predisposed to by numerous environmental factors and affects the entire body. The associated complications are especially common in older patients and those with obesity. The current prevalence of diabetes is high in both developed and developing countries because of changes in lifestyle that have taken place in recent decades. In 2015, more than 415 million adults were estimated to have diabetes, and it has been estimated that by 2040 this number will have increased to 642 million. More than 95% of adult patients with diabetes have type 2 diabetes (T2DM). According to an International Diabetes Federation report, the South Asian region, which comprises Sri Lanka, Bangladesh, Pakistan, India and Nepal, is the epicentre of T2DM.[4] The epidemiology of T2DM and its associated complications, as well as the treatment strategies used, have previously been evaluated in India. This suggested novel, cost-effective treatment strategies for use in low and middle-income countries across the globe.[5]

In recent decades, the prevalence of T2DM and its risk factors have been

thoroughly researched. Dyslipidaemia is common in patients with T2DM and comprises a high plasma concentration of triglycerides (TG), a low concentration of high-density lipoprotein-cholesterol (HDL-c) and a high concentration of low-density lipoprotein-cholesterol (LDL-c), which may cause renal disorders.[6] The analysis of epidemiological data has revealed that disorders in apolipoproteins are associated with T2DM.[7,8] Furthermore, although T2DM is highly heritable, it is also predisposed to by lifestyle factors, including obesity and lack of exercise.[9] We have performed an epidemiological survey in primary hospitals in Anhui Province, China, in which we have shown that lifestyle contributes to the incidence of DM-CKD and identified risk factors that are associated with the prevalence of DM-CKD. On the basis of these findings, we suggest that further targeted preventive measures are required for patients with T2DM and renal complications.

Materials and Methods

Participants

We performed a cross-sectional, retrospective study of patients with T2DM from 12 villages and towns who attended one of five primary hospitals in Anhui Province using a multi-stage sampling method. The inclusion criteria were (1) age 25 to 80 years old, (2) residence and origin in Anhui, and (3) provision of written informed consent. Individuals with mental or physical disorders were excluded from the study. The present study was approved by the Ethics Committee of Anhui Medical University (PJ2018-13-14) and all the data have been de-identified. We confirm that fellow researchers may reproduce our methodology from the description provided.

Survey methods

Questionnaire design. An electronic questionnaire was designed for the Anhui Province Science and Technology Plan to record demographic data (sex, age and ethnicity), the presence of DM, lifestyle and the use of medication. The data collected were reviewed by the investigators to confirm their accuracy.

Physical examination. Physicians and other personnel with appropriate professional training performed physical examinations in designated physical examination institutions using standard procedures. The examination comprised the measurement of height and body mass, ultrasonographic examination of the kidneys, fundic examination, blood pressure measurement and the assessment of blood and urine samples.

Demographic and clinical data, including sex, body mass, age, height and duration of diabetes, were documented. Body mass index (BMI) was calculated as the body mass (kg) divided by the square of the height (m). Blood pressure was measured using standard mercury sphygmomanometers after each participant had been seated for at least 10 minutes. Venous blood samples were drawn and the plasma glucose concentration was measured after an overnight fast (FPG) and 2 hours postprandially (2hPG) using the glucose oxidase technique in the hospital laboratory. The urine albumin/creatinine ratio (UACR) was calculated and recorded in mg/g (1 mg/g = 0.131 mg/mmol).

Diagnosis of chronic kidney disease

CKD was diagnosed if one of the following was identified. (1) Renal injury of $\geq$3 months' duration. Renal injury was defined as abnormal structure or function of the kidney, which was clinically diagnosed on the basis of abnormal nephrological examination, comprising the assessment of

circulating renal indices, urine composition, and ultrasonographic, X-ray, computed tomography, and/or other types of images. (2) eGFR < 60 mL/minute/1.73 m^2 of ≥ 3 months' duration[7] or abnormal urine protein concentration.

Criteria for the identification of potential risk factors

Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg (World Health Organisation 1999 criteria)[10] or the use of antihypertensive medication. Hyperlipidaemia was defined as a serum total cholesterol (TC) concentration > 5.69 mmol/L, a serum triglyceride (TG) concentration > 1.68 mmol/L, a serum HDL-c concentration > 1.03 mmol/L or the use of lipid-lowering medication. Overweight was defined using a BMI between 24 and 27.9 kg/m^2 and obesity was defined using a BMI ≥ 28 kg/m^2, according to the Chinese standards.[11] Renal insufficiency was defined using an eGFR < 60 mL/minute/1.73 m^2. A high glycosylated haemoglobin (HbA1c) was $> 7.0\%$.[12] Hyperuricemia was defined using a plasma uric acid (UA) concentration ≥ 416 mmol/L (≥ 7.0 mg/dL) in men and ≥ 386 mmol/L (≥ 6.5 mg/dL) in women or the use of allopurinol to lower the circulating UA concentration.[13] "Older" patients were defined as being > 65 years old.[14] A normal FPG was defined as ≥ 7.0 mmol/L and a normal 2hPG as ≤ 11.1 mmol/L.[15,16]

Statistics

Data were recorded using double entry in Epidata 3.0 (https://www.epidata.dk/download.php) and evaluated using SPSS 23.0 (IBM, Inc., Armonk, NY, USA). Continuous data are summarised using means $\pm$ SDs and single-factor analyses were performed using the Mann–Whitney U test. Categorical data are summarised as percentages and were analysed using the chi-square test. We identified factors associated with CM-CKD using factor rotation of maximal orthogonal rotation (maximum variance method). The principal components of the risk factors were named according to the appropriate biochemical criterion, using an absolute value of factor loading of ≥ 0.3. Binary logistic regression analysis was performed to analyse the relationships between DM-CKD and potential risk factors, generating odds ratios (ORs) and 95% confidence intervals (CIs). $P < 0.05$ was regarded as indicating statistical significance. The reporting of the study conformed with the STROBE guidelines.[17]

Results

Prevalence of diabetes mellitus with chronic kidney disease (DM-CKD)

A total of 1207 people were evaluated for the present study, and 1067 gave their written informed consent and met the inclusion criteria (response rate 88.4%). The results of the initial assessment of renal function were that 542 participants (50.8%) showed signs of CKD and required a second assessment, of whom 456 were actually re-assessed (42.7%), meaning that 86 (8.1%) did not complete the study. Three hundred forty-five participants were diagnosed with CKD after re-assessment (32.3%), of whom 65 (18.8%) were in stage 1 CKD, 42 (12.2%) were in stage 2 CKD, 200 (58.0%) were in stage 3 CKD, 34 (9.9%) were in stage 4 CKD, and four (1.2%) were in stage 5 CKD.

Univariate analysis of the relationships of DM-CKD with other factors

The relationships of demographic data (sex, age and ethnicity), physical examination

data (SBP, DBP and BMI), use of medication, type of diabetes, smoking and drinking habits, FPG, 2hPG, HbA1c, renal function, blood urea nitrogen, plasma UA, plasma β2-microglobulin, plasma lipid profile (TC, TG, HDL-c and LDL-c concentrations), urine protein concentration and urine pH with DM-CKD were initially evaluated using univariate analysis. SBP (134 *vs.* 130 mmHg, $P = 0.0001$), fasting plasma glucose (7.82 *vs.* 7.60 mol/L, $P = 0.0544$), triglyceride (1.40 *vs.* 1.31 mmol/L, $P = 0.0121$), 2-hour postprandial plasma glucose (2hPG) (11.4 *vs.* 10.7 mmol/L, $P = 0.0001$), urine protein (2+ *vs.* 1+, $P = 0.0001$), glycated haemoglobin (7.7% *vs.* 7.4%, $P = 0.0390$), blood urea nitrogen (6 *vs.* 5.4 mmol/L), plasma UA (290 *vs.* 264 μmol/L, $P = 0.0001$), plasma β2-microglobulin (187 *vs.* 153 nmol/L, $P = 0.0001$), age (62.4 *vs.* 56.7 years, $P = 0.0001$) and the duration of diabetes (10.13 *vs.* 7.77 years, $P = 0.0001$) were found to be significantly associated. These data are presented in Tables 1 and 2.

Multivariate analysis to identify factors associated with DM-CKD

Parameters that were statistically significant in the univariate analysis were used in backward stepwise logistic regression analysis, with DM-CKD as the dependent variable and an alpha of 0.05, to identify factors that might influence the prevalence of DM-CKD. This analysis showed that age, SBP, the duration of diabetes, plasma UA concentration and 2hPG were associated with the incidence of DM-CKD, and after adjustment for covariates, all of these remained significant, as shown in Table 3. We also investigated the effect of sex on the incidence of DM-CKD, as shown in Table 4, and the interactions between the duration of diabetes and other parameters are shown in Table 5. We found that the longer is the duration of diabetes, the stronger are the interactions with high blood glucose, high glycated haemoglobin, high triglyceride, high cholesterol, hypertension, high BMI and high uric acid, which predispose towards diabetic nephropathy.

Duration of diabetes interacts with other parameters in patients with DM-CKD

Analyses of the interactions between the duration of diabetes and other parameters revealed that after adjustment for covariates, a long duration of diabetes and obesity was associated with an odds ratio (OR) (95% confidence interval [CI]) of 2.40 (1.41, 4.07) *versus* a short duration and normal BMI. Compared with a short duration of diabetes and low FPG, the OR (95% CI) for a long duration of diabetes and high FPG was 2.77 (1.86, 4.14), and that for a long duration of diabetes and high FPG was 3.75 (2.55, 5.51). The OR (95% CI) for a long duration of diabetes and high FPG was 2.77 (1.86, 4.14) *versus* a short duration of diabetes and low 2hPG. Compared with a short duration of diabetes and low HbA1c, the OR (95% CI) for a long duration of diabetes and high HbA1c was 2.27 (1.59, 3.26). Compared with a short duration of diabetes and low TG concentration, the OR (95% CI) for a long duration of diabetes and high TG concentration was 3.65 (2.42, 5.51). Finally, compared with a short duration of diabetes and low TC concentration, the OR (95% CI) for a long duration of diabetes and high TC concentration was 2.11 (1.21, 3.68). Thus, long duration of diabetes showed multiple positive interactions: with BMI, FPG, 2hPG, HbA1c, TG, TC, HDL-c and UA (Table 6).

Classification of risk factors and relationships of three key potential risk factors with DM-CKD

Principal components analysis yielded a Kaiser–Mayer–Olkin value of 0.414,

Table 1. Results of the univariate analyses of the relationships of type 2 diabetes and chronic kidney disease with parameters described using continuous data.

Parameter	Presence of diabetes and chronic kidney disease		Statistic*	*P*-value
	No	Yes		
BMI				
N	722	345	0.03	0.85
Mean ± SD	24.64 ± 3.68	24.55 ± 3.73		
Median (min, max)	24.50 (14.45, 40.09)	24.34 (13.68, 40.06)		
Systolic blood pressure				
N	722	345	22.87	<0.0001
Mean ± SD	130.25 ± 20.87	135.77 ± 23.81		
Median (min, max)	130 (70, 434)	134 (60, 402)		
FPG concentration				
N	722	345	3.70	0.054
Mean ± SD	8.41 ± 4.39	8.86 ± 5.91		
Median (min, max)	7.6 (4, 85)	7.82 (2.4, 87)		
TC concentration				
N	722	345	0.01	0.91
Mean ± SD	4.51 ± 1.03	4.54 ± 1.17		
Median (min, max)	4.48 (0.98, 10.67)	4.49 (1.88, 9.09)		
TG concentration				
N	722	345	6.29	0.01
Mean ± SD	1.6 ± 1.23	1.94 ± 1.97		
Median (min, max)	1.31 (0.37, 18)	1.4 (0.29, 17.35)		
HDL-c concentration				
N	722	345	0.006	0.93
Mean ± SD	1.34 ± 0.34	1.34 ± 0.36		
Median (min, max)	1.29 (0.52, 3.32)	1.29 (0.51, 3.07)		
LDL-c concentration				
N	722	345	0.86	0.35
Mean ± SD	2.7 ± 0.9	2.67 ± 1		
Median (min, max)	2.69 (0.61, 7.86)	2.57 (0.65, 5.93)		
Urine pH				
N	722	345	0.49	0.48
Mean ± SD	5.49 ± 2.49	5.85 ± 4.88		
Median (min, max)	5 (1.02, 50)	5 (4, 60)		
2hPG concentration				
N	722	345	11.35	0.0008
Mean ± SD	11.62 ± 6.31	12.1 ± 3.9		
Median (min, max)	10.7 (1.4, 151)	11.4 (1.9, 32.9)		
Urine protein concentration**				
N	722	345	225.56	<0.0001
Mean ± SD	1.31 ± 0.7	2.45 ± 1.38		
Median (min, max)	1 (1, 6)	2 (1, 5)		
Glycosylated haemoglobin				
N	722	345	4.26	0.04
Mean ± SD	8.28 ± 6.14	8.18 ± 2.87		
Median (min, max)	7.4 (1.3, 86)	7.7 (1.9, 47)		

(continued)

Table 1. Continued.

Parameter	Presence of diabetes and chronic kidney disease		Statistic*	*P*-value
	No	Yes		
Blood urea nitrogen				
N	722	345	39.20	<0.0001
Mean ± SD	5.6 ± 1.63	6.87 ± 3.42		
Median (min, max)	5.4 (1.2, 23)	6 (1.8, 32.6)		
Plasma uric acid concentration				
N	722	345	25.08	<0.0001
Mean ± SD	273.8 ± 82.1	306.8 ± 102.6		
Median (min, max)	264 (87.4, 592)	290 (26.0, 691)		
Plasma β2-MG concentration				
N	722	345	98.33	<0.0001
Mean ± SD	1.93 ± 0.75	2.79 ± 2.07		
Median (min, max)	1.8 (1.0, 14.9)	2.2 (1.0, 20)		
Diastolic blood pressure				
N	722	345	0.15	0.6931
Mean ± SD	82.16 ± 14.14	84.67 ± 46.43		
Median (min, max)	80 (28, 176)	80 (20, 901)		
Age				
N	722	345	29.70	<0.0001
Mean ± SD	57.7 ± 10.9	61.7 ± 11.2		
Median (min, max)	56.66 (23.6, 107.1)	62.37(23.7, 97.9)		
Duration of diabetes				
N	722	345	54.74	<0.0001
Mean ± SD	9.33 ± 5.46	11.63 ± 5.74		
Median (min, max)	7.77 (0.01, 39.66)	10.13 (0.17, 36.56)		

*Mann–Whitney U test. **The data were categorised as 1 (<0.1 g/L), 2 (0.1–0.2 g/L), 3 (0.2–1.0 g/L), 4 (1.0–2.0 g/L, 5 (2.0–4.0 g/L or 6 (>4.0 g/L).

BMI, body mass index, FPG, fasting plasma glucose; TC, total cholesterol; TG, triglyceride; HDL-c, high-density lipoprotein-cholesterol; LDL-c, low-density lipoprotein-cholesterol; 2hPG, 2-hour postprandial plasma glucose; β2MG, β2-microglobulin.

$P < 0.01$ in Bartlett's Test of Sphericity. Principal components analysis with a characteristic root > 1 and a scree plot identified three common factors with a cumulative contribution rate of 50.1%. Table 6 shows the rotated component matrix for the three potential risk factors identified in exploratory factor analysis. These three risk factors were renal function, plasma lipid profile and plasma glucose concentration, according to the absolute values of factor load.

Table 7 shows the results of logistic regression analysis for the three potential risk factors for DM-CKD. Renal function and plasma glucose concentration were significantly positively associated with DM-CKD (adjusted ORs (95% CIs) 6.46 (4.79, 8.70) and 1.19 (1.03, 1.37), respectively) after adjustment for confounding variables. However, no relationship between plasma lipid profile and DM-CKD was identified.

Discussion

Changes in lifestyle during recent decades have led to diabetes becoming the most

Table 2. Results of univariate analyses of the relationships of type 2 diabetes and chronic kidney disease with parameters described using categorical data.

	Presence of diabetes and chronic kidney disease			
Parameter	No	Yes	χ^2	*P*-value
Alcohol consumption				
Yes	114 (17.5%)	45 (6.9%)	1.23	0.5382
No	327 (50.3%)	159 (24.5%)		
Unknown	3 (0.46%)	2 (0.31%)		
Type of diabetes				
Type 1 diabetes	7 (0.68%)	5 (0.48%)	0.49	0.4822
Type 2 diabetes	695 (67.1%)	329 (31.8%)		
Smoker				
Yes	117 (17.9%)	58 (8.9%)	0.14	0.9295
No	325 (49.8%)	150 (23.0%)		
Unknown	2 (0.31%)	1 (0.15%)		
Previous use of medication				
Yes	703 (66.9%)	332 (31.6%)	0.36	0.5469
No	12 (1.1%)	4 (0.38%)		
Ethnicity				
Han	716 (67.2%)	343 (32.2%)	0.67	0.4115
Other	5 (0.47%)	1 (0.09%)		
Sex				
Female	364 (34.1%)	166 (15.6%)	0.49	0.4822
Male	358 (33.6%)	179 (16.8%)		

frequent cause of CKD and ESRD. Furthermore, in some hospitals, and particularly in primary hospitals, the majority of patients are diagnosed with severe diabetes, accompanied by complications, and particularly renal complications of diabetes. Therefore, it is necessary to increase the awareness of healthcare professionals regarding DM-CKD and to ensure that the kidney function of patients with diabetes is regularly checked to help prevent or delay the development of CKD. In the present study, we assessed the renal function of patients with diabetes who were attending primary hospitals in Anhui Province, China, and found that the prevalence of DM-CKD was 32.3%, which is higher than that identified in a study by Damtie *et al.* that was performed in Northwest Ethiopia (21.3%).[18] Furthermore, a study performed in Shanghai showed prevalences of albuminuria and CKD in patients with T2DM of 25.2% and 27.1%, respectively, and the prevalence of a slight impairment in kidney function (eGFR $<60\,mL/min/1.73\,m^2$) was 6%.[19] The higher prevalence of DM-CKD in the present study might be explained by differing lifestyle and dietary habits of patients attending primary hospitals in Anhui, but these factors require further investigation.

The prevalence of DM-CKD is high worldwide, and to reduce this, potential risk factors for diabetes and its complications must be identified. Age, SBP, TG concentration, urine protein concentration, plasma β2-microglobulin concentration, and the duration of diabetes in patients

Table 3. Odds ratios for potential risk factors for diabetes complicated by chronic kidney disease.

Parameter	Crude OR	Adjusted OR
BMI		
Obese	0.85 (0.58, 1.24)	0.89 (0.61, 1.31)
Overweight	0.94 (0.70, 1.27)	1.01 (0.75, 1.37)
Normal weight	1.0	1.0
SBP		
High	**1.74 (1.32, 2.31)**	**1.72 (1.29, 2.29)**
Low	1.0	1.0
TG		
High	**1.50 (1.12, 2.0)**	**1.57 (1.18, 2.10)**
Low	1.0	1.0
FPG		
High	1.05 (0.74, 1.45)	1.07 (0.77, 1.48)
Low	1.0	1.0
2hPG		
High	**1.63 (1.23, 2.16)**	**1.66 (1.25, 2.22)**
Low	1.0	1.0
Duration of diabetes		
>10 years	**2.21 (1.68, 2.90)**	**1.96 (1.48, 2.59)**
≤10 years	1.0	1.0
Hb1Ac		
High	1.01 (0.74, 1.36)	0.97 (0.70, 1.33)
Low	1.0	1.0
TC		
High	1.25 (0.85, 1.84)	1.29 (0.88, 1.91)
Low	1.0	1.0
HDL-c		
High	1.0	1.0
Low	1.10 (0.88, 1.56)	1.15 (0.81, 1.65)
UA		
High	**3.54 (1.81, 6.94)**	**3.36 (1.70, 6.66)**
Low	1.0	1.0
Age		
≥65 years old	**1.64 (1.25, 2.15)**	**1.64 (1.25, 2.16)**
<65 years old	1.0	1.0

Significant results are shown in bold ($P < 0.01$).

OR, odds ratio; BMI, body mass index; SBP, systolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; TC, total cholesterol; HbA1c, glycosylated haemoglobin; HDL-c, high-density lipoprotein-cholesterol; 2hPG, 2-hour postprandial plasma glucose; UA, uric acid.

with DM-CKD were identified as potential risk factors in the present study. We found that the prevalence of DM-CKD was higher in older people. A previous study showed a different relationship between the duration of diabetes and DM-CKD, that UA is an independent risk factor for early-onset T2DM, and that SBP and TG are independent risk factors for late-onset T2DM. The duration of diabetes and SBP were also found to be independent risk factors for diabetic retinopathy during

Table 4. Odds ratios for potential risk factors for diabetes complicated by chronic kidney disease, analysed according to sex.

	Male		Female	
Parameter	Crude OR	Adjusted OR	Crude OR	Adjusted OR
BMI				
Obese	0.77 (0.44, 1.36)	0.87 (0.49, 1.57)	0.90 (0.54, 1.50)	0.90 (0.61, 1.31)
Overweight	0.83 (0.54, 1.27)	0.90 (0.59, 1.39)	1.07 (0.70, 1.63)	1.01 (0.75, 1.37)
Normal weight	1.0	1.0	1.0	1.0
SBP				
High	**1.72 (1.15, 2.56)****	**1.74 (1.16, 2.62)****	**1.80 (1.20, 2.68)****	**1.74 (1.16, 2.60)***
Low	1.0	1.0	1.0	1.0
TG				
High	1.47 (0.97, 2.22)	**1.59 (1.04, 2.43)***	**1.56 (1.04, 2.32)***	**1.63 (1.09, 2.45)***
Low	1.0	1.0	1.0	1.0
FPG				
High	1.08 (0.68, 1.72)	1.05 (0.65, 1.68)	1.02 (0.65, 1.61)	1.07 (0.77, 1.48)
Low	1.0	1.0	1.0	1.0
2hPG				
High	**1.74 (1.16, 2.61)****	**1.84 (1.21, 2.79)****	**1.53 (1.02, 2.28)***	**1.53 (1.02, 2.28)***
Low	1.0	1.0	1.0	1.0
Duration of diabetes				
>10 years	**1.98 (1.34, 2.92)****	**1.76 (1.18, 2.63)****	**2.47 (1.69, 3.62)****	**2.18 (1.46, 3.23)****
≤10 years	1.0	1.0	1.0	1.0
Hb1Ac				
High	1.12 (0.71, 1.76)	1.06 (0.66, 1.70)	0.91 (0.59, 1.40)	0.87 (0.56, 1.35)
Low	1.0	1.0	1.0	1.0
TC				
High	1.20 (0.66, 2.18)	1.28 (0.70, 2.36)	1.26 (0.76, 2.09)	1.29 (0.77, 2.14)
Low	1.0	1.0	1.0	1.0
HDL-c				
High	1.0	1.0	1.0	1.0
Low	0.84 (0.53, 1.32)	0.85 (0.54, 1.35)	**1.84 (1.04, 3.25)***	**1.91 (1.07, 3.42)***
Age				
≥65 years old	**1.74 (1.17, 2.57)****	**1.71 (1.15, 2.54)****	**1.55 (1.07, 2.26)***	**1.59 (1.09, 2.31)***
<65 years old	1.0	1.0	1.0	1.0

Significant results are shown in bold (*$P < 0.05$, **$P < 0.01$).
OR, odds ratio; BMI, body mass index; SBP, systolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; TC, total cholesterol; HbA1c, glycosylated haemoglobin; HDL-c, high-density lipoprotein-cholesterol; 2hPG, 2-hour postprandial plasma glucose; UA, uric acid.

early-onset T2DM, and the duration of diabetes, SBP and HbA1c were fund to be independent risk factors during late-onset T2DM.[20] Hypertension and hyperlipidaemia have been shown not only to be risk factors for diabetes complicated by CKD, but also for progression of the disease. Furthermore, dyslipidaemia, hyperglycaemia and hyperuricemia are components of the metabolic syndrome and may indicate the presence of insulin resistance.[21] The mechanisms of hypertension and hyperlipidaemia involve salt retention, overactivation of the renin-angiotensin system and

Table 5. Interactions between the duration of diabetes and other potential risk factors for diabetes complicated by chronic kidney disease.

Parameter	Crude OR	Adjusted OR
Duration of diabetes × FPG		
Long duration × high FPG	**2.77 (1.86, 4.14)**	**2.56 (1.71, 3.84)**
Long duration × low FPG	**2.37 (1.44, 3.87)**	**2.16 (1.31, 3.56)**
Short duration × high FPG	1.32 (0.90, 1.95)	1.37 (0.93, 2.03)
Short duration × low FPG	1.0	1.0
Duration of diabetes × 2hPG		
Long duration × high 2hPG	**3.75 (2.55, 5.51)**	**3.41 (2.32, 5.02)**
Long duration × low 2hPG	**2.07 (1.41, 3.03)**	**1.79 (1.20, 2.67)**
Short duration × high 2hPG	**1.57 (1.10, 2.25)**	**1.58 (1.10, 2.26)**
Short duration × low 2hPG	1.0	1.0
Duration of diabetes × Hb1Ac		
Long duration × high Hb1Ac	**2.27 (1.59, 3.26)**	**2.20 (1.50, 3.22)**
Long duration × high Hb1Ac	**1.92 (1.24, 2.97)**	**1.84 (1.14, 2.99)**
Short duration × high Hb1Ac	0.98 (0.69, 1.40)	1.10 (0.76, 1.60)
Short duration × high Hb1Ac	1.0	1.0
Duration of diabetes × TC		
Long duration × high TC	**2.11 (1.21, 3.68)**	**1.99 (1.13, 3.49)**
Long duration × low TC	**2.55 (1.91, 3.39)**	**2.26 (1.69, 3.04)**
Short duration × high TC	**2.24 (1.39, 3.61)**	**2.36 (1.46, 3.82)**
Short duration × low TC	1.0	1.0
Duration of diabetes × TG		
Long duration × high TG	**3.65 (2.42, 5.51)**	**3.47 (2.29, 5.25)**
Long duration × low TG	**2.04 (1.47, 2.84)**	**1.79 (1.28, 2.51)**
Short duration × high TG	1.38 (0.96, 1.98)	1.44 (1.00, 2.08)
Short duration × low TG	1.0	1.0
Duration of diabetes × SBP		
Long duration × high SBP	**3.95 (2.63, 5.94)**	**3.51 (2.32, 5.31)**
Long duration × low SBP	**2.25 (1.62, 3.14)**	**2.02 (1.44, 2.84)**
Short duration × high SBP	**1.83 (1.27, 2.64)**	**1.84 (1.28, 2.67)**
Short duration × low SBP	1.0	1.0
Duration of diabetes × BMI		
Long duration × obesity	**2.52 (1.49, 4.26)**	**2.40 (1.41, 4.07)**
Long duration × overweight	**1.95 (1.25, 3.04)**	**1.77 (1.13, 2.78)**
Long duration × normal weight	**2.63 (1.77, 3.91)**	**2.40 (1.61, 3.59)**
Short duration × obesity	1.09 (0.66, 1.82)	1.12 (0.68, 1.87)
Short duration × overweight	1.22 (0.82, 1.80)	1.32 (0.89, 1.96)
Short duration × normal weight	1.0	1.0
Duration of diabetes × HDL		
Long duration × low HDL	**2.04 (1.20, 3.44)**	**1.87 (1.10, 3.19)**
Long duration × high HDL	**2.32 (1.74, 3.09)**	**2.06 (1.54, 2.77)**
Short duration × low HDL	1.30 (0.82, 2.06)	1.36 (0.85, 2.17)
Short duration × high HDL	1.0	1.0
Duration of diabetes × UA		
Long duration × high UA	**9.70 (3.45, 27.41)**	**8.5 (3.0, 24.24)**
Long duration × low UA	**2.21 (1.50, 3.26)**	**2.0 (1.34, 2.98)**

(continued)

Table 5. Continued.

Parameter	Crude OR	Adjusted OR
Short duration × high UA	2.43 (0.93, 6.38)	2.36 (0.90, 6.21)
Short duration ×low UA	1.0	1.0

Significant results are shown in bold ($P < 0.01$).
The definitions of the categories used: long duration, >10 years; short duration, ≤years; high FPG, >7.0 mmol/L; low FPG, ≤7.0 mmol/L; high 2hPG, >11.1 mmol/L; low 2hPG, ≤11.1 mmol/L; low HbA1c, ≤7.0%; high HbA1c, >7.0%; low TC, ≤5.69 mmol/L; high TC, >5.69 mmol/L; low TG, ≤1.68 mmol/L; high TG, >1.68 mmol/L; low HDL, ≤1.03 mmol/L; high HDL, >1.03 mmol/L; low UA, < 416 mmol/L in men and < 386 mmol/L; high UA ≥ 416 mmol/L in men and ≥386 mmol/L in women.
OR, odds ratio; BMI, body mass index; SBP, systolic blood pressure; FPG, fasting plasma glucose; TG, triglyceride; TC, total cholesterol; HbA1c, glycosylated haemoglobin; HDL-c, high-density lipoprotein-cholesterol; 2hPG, 2-hour postprandial plasma glucose; UA, uric acid.

Table 6. Rotated component matrix for three risk factors in an exploratory factor analysis.

	Risk factor		
Parameter	Factor 1 (Renal function)	Factor 2 (Plasma lipid profile)	Factor 3 (Plasma glucose concentration)
β2-microglobulin	0.843		
Blood urea nitrogen	0.809		
Albumin/creatinine ratio	0.750		
Urine protein concentration	0.660		
Uric acid	0.532		
Total cholesterol		0.984	
Low-density lipoprotein-cholesterol		0.879	
High-density lipoprotein-cholesterol		0.401	
Triglyceride		0.304	
2-hour postprandial blood glucose			0.711
Fasting plasma glucose			0.703
Glycosylated haemoglobin			0.497

Extraction method: principal component analysis. Rotation method: varimax with Kaiser normalisation.

Table 7. Logistic regression models for the association between latent risk factors and profiles of diabetes combined with chronic kidney disease.

	Crude OR	Adjusted OR
Factor 1 (Renal function)	5.80 (4.39, 7.68)**	6.46 (4.79, 8.70)**
Factor 2 (Plasma lipid profile)	0.99 (0.85, 1.16)	0.95 (0.81, 1.11)
Factor 3 (Plasma glucose concentration)	1.20 (1.04, 1.37)*	1.19 (1.03, 1.37)*

OR, odds ratio. *$P < 0.05$; **$P < 0.01$.

high sympathetic nerve activity. Therefore, adherence to a low-salt, low-fat diet and regular measurements of blood pressure, circulating glucose and lipid concentrations, and other parameters have the potential to reduce the incidence of CKD.[22,23] Furthermore, screening of renal function and appropriate interventions

should be performed early in patients with T2DM to prevent further deterioration of renal function and the progression to ESRD.

In the present study, we studied the interactions between the duration of diabetes and other parameters with respect to the risk of DM-CKD, and found that a long duration of diabetes is associated with BMI, FPG, 2hPG, HbA1c, TG, TC, UA and HDL-c. in individuals with DM-CKD, and that as the duration of diabetes increases, the likelihood of having a complication increases.[15,24] Previous studies have shown that the progression of nephropathy in older patients with long-standing diabetes is significantly faster than in older patients who have had diabetes for <5 years.[14] In addition, older patients who have had diabetes for ≥ 10 years were shown to be at higher risk of the progression of nephropathy.[14] In the present study, we have shown that the duration of diabetes is associated with many risk factors, which has also been shown previously.[25] In recent years, "metabolic memory" has become a major area of interest in diabetes research, and patients that experience hyperglycaemia over a long period are at a higher risk of microvascular disease.[26–28] Furthermore, a reduction in hyperglycaemia has been shown to prevent damage to microvessels.[29] The findings of the Diabetes Control and Competition Trial[30] were also consistent with the results of these previous studies.

UA is synthesised through redox reactions catalysed by xanthine oxidoreductase and predisposes towards the formation of macrophage foam cells, which contributes to the pathogenesis of DN.[31] The present findings are consistent with the results of other studies which showed that plasma UA concentration correlates with the progression of kidney disease in patients with T2DM, and that it is predictive of nephropathy, even when at a normal concentration of $< 375\,\mu mol/L$.[32–34] UA is the end product of purine catabolism in humans, and $\sim$70% is excreted through the kidneys.[35] Previous studies have shown that a high circulating UA concentration is associated with risk factors for T2DM,[36] hypertension,[37] cardiovascular disease,[38] and metabolic syndrome.[39] It has been reported that UA may be involved in the pathogenesis of DN by promoting microvascular disease, through mechanisms such as endothelial dysfunction,[40] activation of the renin-angiotensin-aldosterone system,[41] activation of proinflammatory pathways[41] and greater secretion of profibrotic cytokines.[42]

An abnormal plasma lipid profile has been shown to be associated with the development and progression of both diabetes and renal disease,[19] and we made consistent findings in the present study. This is because high TC, TG and LDL-c concentrations and a low HDL-c concentration in patients with diabetes are associated with macrovascular complications.[43] Circulating glucose and HbA1c are used to monitor patients with diabetes and high levels are associated with both micro and macrovascular complications[13]. The duration of diabetes, poor glycaemic control and older age have been shown to significantly contribute to mortality in patients with diabetes.[44] Numerous previous studies have shown that the risk of diabetic complications is associated with a long duration of hyperglycaemia, as well as its severity[45,46], but that this is sex-specific.[47] The Systolic Blood Pressure Intervention Trial led to the development of guidelines that recommended the control of blood pressure in patients with CKD and diabetes.[48] Furthermore, another study revealed that microvascular complications in patients with type 1 diabetes occur in clusters. For example, neuropathy is associated with an OR (95% CI) of 2.15 (1.73, 2.66) for CKD and retinopathy is associated with ORs

(95% CIs) of 2.49 (1.92, 3.24) for DKD and 2.66 (1.94–3.64) for neuropathy.[49]

Limitations and strengths of the present study

In the present study, multi-stage sampling was used to evaluate the prevalence of T2DM with CKD and to identify potential risk factors in patients attending primary hospitals in Anhui Province, China. The risk factors identified using principal components analysis fit well with the natural history of patients with DM-CKD. However, the study was limited by the availability of gold-standard laboratory testing and a small sample size. In addition, this was a cross-sectional study; therefore, it is not possible to ascribe causal relationships to the associations identified. Therefore, regular follow-up studies should be performed to further investigate the aetiology of the CKD and to evaluate potential treatment plans.

Conclusion

DM-CKD is frequently associated with a poor quality of life, and timely identification of potential risk factors may help improve this situation. We have investigated the relationships between potential risk factors and DM-CKD, and the findings improve our understanding of the importance of these factors for the prevention of diabetic complications. We found that the duration of diabetes was associated with a number of metabolic indices (BMI, SBP, TG and FPG), which implies that monitoring of these parameters may aid the prevention of CKD and other complications of diabetes.

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Author contributions

YXL and QZ designed the study. SQZ and HLH recruited the participants. LLC, FD and TJ performed the statistical analysis. YXL and QZ were responsible for the critical revision of the manuscript. LX and CL drafted and revised the manuscript. All the authors contributed to the manuscript and approved its final version.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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