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# Prevalence and risk factors associated with chronic kidney disease in an adult population from southern China

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## Abstract

**Background.** Population-based studies evaluating the prevalence of kidney damage in different communities have been limited in developing countries. We conducted a population-based screening study in the southern Chinese city of Guangzhou that aimed to identify the prevalence and associated risk factors of chronic kidney disease (CKD) in southern Chinese populations.

**Methods.** We interviewed 6311 residents (>20 years) from six districts of Guangzhou from July 2006 to June 2007 and tested for haematuria, albuminuria and reduced renal function. Associations between age, gender, smoking, diabetes mellitus, hypertension, hyperuricaemia and kidney damage were examined.

**Results.** There were 6311 subjects enrolled in this study. After adjustment for age and gender, the prevalence of albuminuria, haematuria and reduced estimated glomerular filtration rate (eGFR) was 6.6% [95% confidence interval (CI): 5.5–7.6%], 3.8% (95% CI: 3.4%, 4.3%) and 3.2% (95% CI: 2.4%, 3.3%), respectively. Approximately 12.1% (95% CI: 11.3%, 12.9%) of the sample population had at least one indicator of kidney damage. Age, diabetes mellitus, hypertension, central obesity, hyperlipidaemia and use of nephrotoxic medications were independently associated with albuminuria; hyperuricaemia, age, gender, hypertension and use of nephrotoxic medications were independently associated with reduced eGFR, and female gender was independently associated with haematuria.

**Conclusions.** In the general adult population from southern China, 12.1% has either proteinuria, haematuria and/or reduced eGFR, indicating the presence of kidney damage, with an awareness of only 9.6%. The high prevalence and low awareness of CKD in this population suggest an urgent need for CKD prevention programmes in China.

**Keywords:** chronic kidney disease; epidemiology; screening

## Introduction

The prevalence of chronic kidney disease (CKD) is increasing rapidly worldwide, and is now recognized as a global public health problem. In addition, end-stage renal disease

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(ESRD) is at epidemic levels and has become an important health-threatening condition just behind cardiovascular disease, cerebrovascular disease, cancer and diabetes. In the United States and Australia, ∼11–16% of the general population is affected by various renal diseases [1,2]. Studies from Europe have also shown a high prevalence of CKD in the general population [3]. The incidence of ESRD is increasing, with a doubling in the number of patients treated for ESRD in Europe and the United States over the past decade [4,5].

The burden of renal disease is likely to escalate since both population age and prevalence of diabetes are projected to increase dramatically. However, studies examining the prevalence of CKD and its associated factors in developing countries, especially in Chinese populations, remain limited. The prevalence of CKD in China, which has the largest world population, will have a vital influence on global CKD epidemiology. Nevertheless, there have been only a few epidemiological studies that examined CKD prevalence in China. In 2005, Chen *et al.* [6] reported that the prevalence of decreased kidney function was 2.53% in a nationwide representative population of Chinese; however, other indicators of renal injury were not reported. Zhang *et al.* [7] showed that the prevalence of CKD in Chinese aged 40 years or older was 9.4% in a district of Beijing. A more recent study found that the prevalence of CKD in adult Chinese of Beijing was 13.0% [8]. Importantly, the awareness of CKD prevalence among these patients was <10% [6–8]. Three studies from China reported that hypertension and diabetes are the two primary factors associated with CKD [6–8].

Because little is known about the prevalence of CKD in other areas of China, we performed a population-based survey to investigate the prevalence of CKD and its associated factors in a southern Chinese population. The protocols used in our study followed the recommendations of KDIGO (Kidney Disease: Improved Global Outcomes) [9], but were modified because the leading cause (49.9%) of ESRD is glomerulonephritis in China. Accordingly, CKD was defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 $m^2$, irrespective of cause. Kidney damage was ascertained by the presence of albuminuria, defined as the albumin-to-creatinine ratio (ACR) >30 mg/g in a morning urine specimen or haematuria (abnormal: ≥1+) confirmed by urine microscopy [abnormal: ≥3 red blood cells/high-power field (HPF)]. GFR was estimated using the Modification of Diet in Renal Disease (MDRD) study equation modified for the Chinese population [9].

## Subjects and methods

### *Study population*

This study was a cross-sectional examination of CKD and associated risk factors in the general adult population from the city of Guangzhou in southern China (population, >1.1 million) from July 2006 to June 2007. Subjects were local residents aged 20 years or older who had lived in the region for 5 years or longer. Participants were selected using a stratified, multistage sampling method. In the first stage, a total of six districts were sampled from the entire city, consisting of four randomly selected districts from older suburbs and two districts from recently developed suburbs. In the second stage, seven street offices were randomly chosen from each selected district. In the third stage, 12 communities were randomly selected. In the final stage, a simple randomized method was used to select households. In the selected households, all subjects fulfilling the inclusion criteria were selected, until the required number of subjects for each age group was reached.

Using this method, a total of 6311 subjects aged 20 years or older were selected from 12 primary sampling units and were enrolled into the study; of these subjects, 6101 completed the entire survey with a response rate of 96.7%. The study was approved by the Human Ethics Committees of Sun Yat-sen University (Guangzhou, China). Written informed consent was obtained from all participants of this study.

### *Screening protocol and evaluation criteria*

All Staff participating in this study including clinical doctors and medical students received intensive training on proper methods for screening. Data were collected at local health stations or community clinics. A questionnaire documenting socio-demographic status (e.g. age, sex, income and education level), personal and family health history (e.g. hypertension, diabetes and kidney disease) and lifestyle behavior (e.g. smoking) was completed by each subject. History of taking medications with nephrotoxic potential (including non-steroidal anti-inflammatory drugs and herbs containing aristolochic acid) was also recorded.

Anthropometric measurements were obtained using standard protocols and techniques. After removal of shoes and heavy clothing, each subject underwent body weight and height measurements, using a calibrated scale. The body mass index (BMI) was calculated as weight (in kilograms) divided by height squared (in square meters). Venous blood was collected after an overnight fast of at least 10 h for measurements of various biomarkers. A clean-catch, midstream, morning urine specimen was collected for dipstick urinalysis (Roche Diagnostics, Mannheim, Germany) and microscopic analysis. All blood and urine samples were tested in the laboratory of The First Affiliated Hospital, Sun Yat-sen University.

*Albuminuria.* Urinary albumin and creatinine were measured from a morning urine sample using an automatic analyser (COBAS INTEGRA 400 plus, Roche, Basel, Switzerland). Creatinine was measured by Jaffe's kinetic method and albumin by the immunoturbidimetic method. Urinary ACR (mg/g) was calculated. Microalbuminuria and macroalbuminuria were defined as an increase in ACR between 30 and 299 mg/g and 300 mg/g or greater, respectively, according to the guideline of American Diabetes Association. The term 'albuminuria' is used to describe the presence of either microalbuminuria or macroalbuminuria.

*Estimated glomerular filtration rate (eGFR).* Blood was collected by venous puncture after overnight fasting. Serum creatinine (Scr) was measured using the same method as

that for urinary creatinine determination. The eGFR was calculated using the MDRD equation, which was modified for data from Chinese CKD patients [10]. As part of this, 38 serum samples with a creatinine range of 0.5–15 mg/dL were sent to the central laboratory of Peking University First Hospital where the modified equation was developed [10]. The resulting calibration equation was ($R^2 = 0.999$): Calibrated Scr (mg/dL) = 0.893 × Scr (mg/dL) + 0.39.

Reduced renal function was defined as an eGFR <60 mL/min/1.73 m$^2$: eGFR (mL/min/1.73 m$^2$) = 175× Calibrated-Scr (mg/dL)$^{-1.234}$ × age (year) $^{-0.179}$ [female×0.79]

*Haematuria.* Dipstick testing (Roche Diagnostics, Mannheim, Germany) of morning spot urine samples was performed. Subjects with haematuria of 1+ or greater were confirmed by microscopic analysis within 2 h. Urine samples were centrifuged at 1500 *g* for 5 min, the supernatant was removed and the sediment in the remaining supernatant was resuspended. An aliquot (20 μL) of the sample was placed on a clean glass slide and examined using subdued bright-field illumination at original magnification of ×100 and ×400 under a light microscope. Three or more red blood cells/HPF by microscopy were considered abnormal. Women who were actively menstruating were excluded from the urine test.

*Hypertension status.* Arterial blood pressure (BP) was measured using a mercury sphygmomanometer after subjects had sat and rested for at least 15 min. The procedure for measuring BP was according to the Joint National Committee VII criteria (JNC VII) [11]. Three readings were taken at 1-min intervals. The mean of these three measurements was calculated unless the difference between readings was >10 mmHg, in which case the mean of the two closest of the three readings was used. Hypertension was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg, or use of anti-hypertensive medication in the previous 2 weeks irrespective of BP or self-reported diagnosis of high BP and use of anti-hypertensive medication.

*Diabetes status.* Fasting blood glucose was measured enzymatically with a glucose oxidase method (COBAS INTEGRA 400 plus, Roche, Basel, Switzerland). Diabetes was defined as the use of insulin or oral hypoglycaemic agents or a fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) and/or 2-h post-prandial plasma glucose ≥11.1 mmol/L (200 mg/dL).

*Other measurements.* Serum total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides and uric acid were measured by an autoanalyser (COBAS INTEGRA 400 plus, Roche). Hyperuricaemia was defined as a serum uric acid level >7.0 mg/dL. Cardiovascular diseases were reported by subjects from diagnoses originating from doctors or other health professionals, and included congestive heart failure, coronary heart disease, angina, stroke or heart attack. The metabolic syndrome was defined according to the National Cholesterol Education Programme Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (ATP III) criteria.

*Statistical analysis*

Data entry and management were performed using Epidata software, version 3.0 (Epidata Association, Odense, Denmark). All analyses and calculations were performed using SPSS software, version 10.0 (SPSS, Inc., Chicago, IL USA).

Data are presented as means ± standard error for continuous variables and as proportions for categorical variables. Quantitative variables were summarized as means and 95% confidence intervals (CI). Differences between subjects were analysed by two-tailed unpaired Student's *t* tests for continuous data and by $\chi^2$ tests for categorical data. Univariate and multivariate logistic regression analyses were used to estimate odds ratios (OR) and CIs by comparing associated risk factors on CKD occurrence. $P<0.05$ was considered significant. The overall CKD prevalence, defined as the presence of at least one of albuminruia, haematuria or eGFR values <60 (mL/min/1.73 m$^2$), was calculated and tested for interactions with demographic characteristics (i.e. age group, gender, education level, smoking and family history) and with CKD risk factors (diabetes, cardiovascular disease, hypertension and BMI). Estimates analysed by demographic characteristics and by risk factors were age and gender standardized to the Guangzhou standard population aged ≥20 years by using data from the China Population Census in 2000 (http://www.gzstats.gov.cn).

## Results

Of 6311 subjects that were enrolled into the study, 6101 had a complete data set and were entered into the final analysis. The demographic and clinical characteristics of the study population are shown in Table 1. The prevalences of hypertension and diabetes were 19.2 and 5.5%, respectively (Table 1). Interestingly, 4.9% of the population (no gender difference) used potentially nephrotoxic medications that included Chinese herbs such as the *Aristolochia* species.

*Prevalence of indicators of kidney damage*

*Albuminuria.* The overall prevalence of albuminuria was 6.6% (95% CI: 5.5–7.6%, Table 1). Microalbuminuria and macroalbuminuria were detected in 5.8 and 0.8% of participants, respectively. The prevalence of albuminuria was higher in women than men (7.5 versus 6.0%, $P = 0.003$), and increased with age in both genders ($P <0.001$ for both men and women, respectively). The prevalence of albuminuria was higher in the subjects with diabetes or hypertension (15.8 and 11.6%, respectively) compared with those without diabetes or hypertension (4.7 and 5.9%, respectively). The highest prevalence of albuminuria was found in subjects with both diabetes and hypertension (22.5%) compared with those without hypertension and diabetes in which the prevalence of albuminuria was only 3.2%.

*Haematuria.* Haematuria was present in 3.8% (95% CI: 3.4–4.3%, Table 1) of the participants. The prevalence of haematuria was significantly higher in women than men (6.6 versus 2.4%, $P<0.0001$). Notably, 71% of the

**Table 1.** Socio-demographic and clinical characteristics of the study population

| Variable | Total | Male | Female | *P*-value |
|---|---|---|---|---|
| Age (year) | 51.6 ± 12.8 | 53.4 ± 13.1 | 50.7 ± 12.4 | <0.001 |
| Body weight (kg) | 59.3 ± 15.6 | 65.4 ± 10.2 | 56.4 ± 16.8 | <0.001 |
| Serum creatinine (μmol/L) | 69.2 ± 16.6 | 70.6 ± 15.2 | 65.5 ± 12.4 | <0.001 |
| Blood cholesterol (mmol/L) | 5.6 ± 1.2 | 5.6 ± 1.2 | 5.7 ± 1.2 | 0.001 |
| Serum triglyceride (mmol/L) | 1.5 ± 1.0 | 1.7 ± 1.2 | 1.5 ± 1.7 | <0.001 |
| Blood uric acid (μmol/L) | 348.3 ± 93.4 | 402.1 ± 89.6 | 322.9 ± 84.2 | <0.001 |
| Fasting blood glucose (mmol/L) | 5.6 ± 1.5 | 5.6 ± 1.6 | 5.5 ± 1.5 | 0.076 |
| Systolic blood pressure (mmHg) | 123.4 ± 19.9 | 125.1 ± 18.3 | 122.6 ± 20.5 | <0.001 |
| Diastolic blood pressure (mmHg) | 79.1 ± 10.7 | 81.2 ± 10.6 | 78.1 ± 10.6 | <0.001 |
| Body mass index (BMI) | 23.6 ± 5.8 | 23.81 ± 3.3 | 23.5 ± 6.6 | 0.009 |
| ≥High school education (%) | 51.7 | 61.9 | 46.9 | <0.001 |
| Health insurance coverage (%) | 62.9 | 64.8 | 62.1 | 0.04 |
| Income (RMB/month) | 3637.4 | 3843.0 | 3534.2 | 0.001 |
| Smoker (%) | 18.8 | 53.6 | 2.1 | <0.001 |
| History of CKD (%) | 3.2 | 3.1 | 3.2 | 0.83 |
| Family history of diabetes (%) | 16.3 | 15.9 | 16.5 | 0.54 |
| Family history of hypertension (%) | 39.1 | 37.0 | 40.1 | 0.03 |
| Family history of CKD (%) | 4.8 | 4.7 | 4.8 | 0.92 |
| Repeated respiratory tract infections (%) | 18.1 | 20.1 | 17.2 | 0.01 |
| Nephrotoxic medications (%) | 4.9 | 4.7 | 4.8 | 0.92 |
| Central obesity (%) | 30.0 | 20.6 | 40.8 | <0.001 |
| History of acute myocardial infarct (%) | 9.3 | 9.2 | 9.3 | 0.86 |
| Stroke (%) | 2.4 | 2.3 | 2.4 | 0.82 |
| Hypertension (%) | 19.2 | 22.5 | 18.3 | 0.058 |
| Diabetes (%) | 5.5 | 6.0 | 5.2 | 0.215 |
| Hyperlipidaemia (%) | 41.4 | 46.1 | 35.9 | 0.003 |
| Hyperuricaemia (%) | 26.8 | 41.4 | 9.8 | <0.001 |
| Cardiovascular diseases (%) | 7.6 | 7.7 | 7.5 | 0.74 |
| eGFR <60 mL/min/1.73 $m^2$ (%) | 3.2 | 2.2 | 4.1 | <0.001 |
| ACR > 30 mg/g (%) | 6.6 | 6.0 | 7.5 | 0.003 |
| Haematuria (%) | 3.8 | 2.4 | 6.6 | <0.001 |
| CKD (%) | 12.1 | 10.0 | 13.9 | <0.001 |

Data are means ± SD or percentages.
ACR, urinary albumin-to-creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

subjects with haematuria did not have albuminuria or reduced eGFR. Among all the subjects with haematuria, only 26% were women aged younger than 45 years. Among all the subjects with haematuria, 34% had a urinary sediment of >10 red blood cells/HPF and 8% had >25 red blood cells/HPF.

*eGFR.* Of all the participants, 3.2% (95% CI: 2.8–3.7%) had eGFR values <60 mL/min/1.73 $m^2$ (CKD stage 3 or lower, Table 1). The prevalence of eGFR <60 mL/min/1.73 $m^2$ was significantly higher in women than in men (4.1 versus 2.2%, $P = 0.000$), and became larger with increasing age in both genders ($P < 0.001$ for both men and women). The prevalence of reduced eGFR was higher in the subjects with diabetes or hypertension (10.2 and 9.8%, respectively) compared with those without diabetes or hypertension (4.9 and 3.3%, respectively). In the subjects with both diabetes and hypertension, the prevalence of reduced eGFR was 13.2%, which contrasted with a much lower prevalence (2.2%) in subjects without hypertension and diabetes.

### *Prevalence and awareness of CKD*

The overall prevalence of CKD (stages 1–5) was 12.1% (95% CI: 11.3–12.9%, Table 1) after adjustment for age and gender. By disease stage, the prevalence was as follows: stage 1, 4.1%; stage 2, 4.8%; stage 3, 2.8%; stage 4, 0.3% and stage 5, 0.1%. The prevalence of CKD was greater in the subjects with diabetes or hypertension compared with those without diabetes or hypertension (27.3 versus 11.0%, $P = 0.000$; and 23.8 versus 9.6%, $P = 0.000$, respectively). The prevalence was also greater in the subjects with cardiovascular disease or metabolic syndrome compared with those without these diseases (26.4 versus 10.3%, $P = 0.000$; and 22.3 versus 11.8%, $P = 0.000$, respectively). By age group, CKD (all stages) was more prevalent among populations aged ≧ 60 years (23.7%), but was reduced in younger ages (e.g. 14.6% for subjects between 50 and 59 years and 10.4% for subjects between 20 and 29 years). The prevalence was significantly higher in women than in men (13.9 versus 10.0%, $P = 0.000$), and it increased in both genders with age ($P < 0.001$ for women and men across age groups).

An eGFR <60 mL/min/1.73 $m^2$ was observed in 13.6% of subjects with microalbuminuria, and in 31.2% of those with macroalbuminuria. Microalbuminuria and macroalbuminuria were present in 14.9 and 6.2% of subjects with reduced renal function, respectively. The percentage of subjects with microalbuminuria, macroalbuminuria or haematuria increased with the decline in renal function (Table 2).

**Table 2.** Percentage of subjects with albuminuria or haematuria according to the eGFR stage

| eGFR (mL/min/1.73 $m^2$) | Microalbuminuria (%) | Macroalbuminuria) (%) | Haematuria (%) |
|---|---|---|---|
| >90 | 5.1 | 0.4 | 4.9 |
| 60–89 | 6.1 | 1.5 | 3.5 |
| 30–59 | 14.8 | 3.6 | 7.1 |
| 15–29 | 14.3 | 57.1 | 12.8 |
| <15 | 33.3 | 33.3 | 16.7 |

Only 9.6% of subjects with CKD were aware of having CKD. Low awareness rates were observed among different gender and age groups. The awareness rate of CKD was similar in females and males (9.3 versus 10.2%, $P = 0.72$). The awareness rate increased progressively with the decline in renal function. Among the different stages of CKD (stages 1–5), the awareness rate of CKD was 6.5%, 8.5%, 12.3%, 46.7% and 66.9%, respectively. Compared with subjects with diabetes or hypertension only, subjects with both diabetes and hypertension had a higher awareness rate (10.6 and 12.3% versus 20.5%, $P < 0.01$). Subjects with haematuria possessed the lowest awareness rate (5.9%) among all indicators of kidney injury. The main reported primary renal diseases included glomerulonephritis (54.2%), diabetic nephropathy (14.5%), hypertension nephropathy (11.2%) and nephrolithiasis (12.7%).

### *Risk factors associated with CKD*

Table 3 shows the adjusted ORs for factors associated with CKD. Older age, diabetes, hypertension (either high systolic or diastolic BP), hyperuricaemia, central obesity, metabolic syndrome and smoking were independently associated with the occurrence of CKD. A high level of education (at least a high school education) was protective against CKD. When adjusted by all other variables, older age, diabetes, hypertension (either high systolic or diastolic BP), central obesity, use of nephrotoxic medications, metabolic syndrome and hyperlipidaemia were independently associated with albuminuria. Older age, microalbuminuria, use of nephrotoxic medications, hyperuricaemia, hypertension, metabolic syndrome and smoking were independently associated with reduced renal function. Female gender and microalbuminuria were independently associated with the presence of haematuria.

**Table 3.** Adjusted odds ratios for presence of CKD, albuminuria or reduced renal function

| Variable | *P*–value | Adjusted OR (95% CI) |
|---|---|---|
| CKD | | |
| Age (↑ 10 year) | <0.001 | 1.29 (1.19–1.39) |
| Diabetes | 0.007 | 1.37 (1.09–1.71) |
| Hyperuricaemia | <0.001 | 1.60 (1.31–1.96) |
| Hypertension | <0.001 | 1.49 (1.23–1.80) |
| High systolic BP | <0.001 | 1.77 (1.44–2.17) |
| High diastolic BP | 0.001 | 1.42 (1.15–1.75) |
| Smoking | 0.02 | 1.41 (1.06–1.89) |
| Central obesity (BMI) | 0.04 | 1.29 (1.01–1.65) |
| Metabolic syndrome | 0.04 | 1.20 (1.01–1.44) |
| Education | 0.01 | 0.90 (0.84–0.98) |
| Albuminuria | | |
| Age (↑ 10 year) | <0.001 | 1.26 (1.11–1.42) |
| Diabetes | <0.001 | 2.09 (1.52–2.87) |
| Hypertension | <0.001 | 1.91 (1.46–2.50) |
| High systolic BP | <0.001 | 2.20 (1.68–2.87) |
| High diastolic BP | <0.001 | 1.70 (1.29–2.25) |
| Education | 0.005 | 0.84 (0.75–0.95) |
| Haematuria | <0.001 | 6.41 (4.41–9.33) |
| Central obesity | 0.002 | 1.70 (1.21–2.39) |
| Hypertriglyceridaemia | 0.010 | 1.32 (1.06–1.64) |
| Metabolic syndrome | <0.001 | 1.87 (1.41–2.48) |
| Nephrotoxic medications | 0.003 | 2.09 (1.29–3.39) |
| Reduced renal function | | |
| Age (↑ 10 year) | <0.001 | 1.85 (1.62–2.13) |
| Microalbuminuria | <0.001 | 2.48 (1.63–3.77) |
| Hypertension | 0.020 | 1.41 (1.05–1.89) |
| High systolic BP | 0.020 | 1.42 (1.05–1.92) |
| Metabolic syndrome | 0.030 | 1.40 (1.04–1.86) |
| Hyperuricaemia | <0.001 | 4.34 (3.23–5.82) |
| Smoking | 0.048 | 1.44 (1.00–2.07) |
| Nephrotoxic medications | 0.002 | 2.32 (1.05–3.45) |

CKD, chronic kidney disease; BP, blood pressure; BMI, body mass index.

## Discussion

China has both the largest population in the world and a great ethnic diversity. The city of Guangzhou has a population of more than 10 million, and is one of the representative urban centers in southern China. The present population-based study is the first to estimate the prevalence of three key indicators of kidney damage, which include albuminuria, reduced eGFR and haematuria, in Southern China. Our findings indicate that 12.1% adults 20 years or older in Guangzhou city may have at least one indicator of kidney damage. This overall prevalence is very close to that detected in northern Chinese from Beijing (13.0%) [8]. This prevalence is also comparable with that of the AusDiab Kidney study in which about 16% of Australian adults had at least one indicator of kidney damage [1], and with the results (11%) from the Third National Health and Nutrition Examination Survey (NHANES) which was based on albuminuria and/or eGFR <60 mL/min/1.73 $m^2$ [2]. Although the total prevalence is similar among these studies, our population showed differences in the profile of kidney damage compared to the other reports.

While analysing data from NHANES III using the MDRD GFR equation, Clase *et al*. [12] reported that 13.0% adult non-diabetic Americans had a GFR <60 mL/min/1.73 $m^2$, which was an unexpectedly high prevalence. Coresh *et al.* [13] adjusted Scr with that of the Cleveland Lab, and reported a prevalence rate of 4.7%. The AusDiab study from Australia showed that an eGFR of <60 mL/min/1.73 $m^2$ was present in 11.2% of the participants [1]. In our study, the prevalence of reduced eGFR was 3.2%. In 2007, Zhang *et al*. [7] reported that 3.0% (95% CI: 1.2–2.1%) of adults aged 40 years or older from a community in Beijing had eGFR values <60 mL/min/1.73 $m^2$. The same group of authors reported that 1.7% of adults had eGFR values <60 mL/min/1.73 $m^2$ when the study population size was increased to 13 925 [8]. Chen *et al*. [6] reported that 2.53% of Chinese adults aged 35–74 years had reduced renal function in a national representative population. In

our study and the studies by Zhang *et al.* [7,8], eGFR was calculated using a newly modified MDRD equation based on data from the Chinese CKD population [10]. Unlike developed countries, in which the major causes of ESRD are diabetes mellitus and hypertension, the leading cause of ESRD in China remains glomerulonephritis that accounts for 49.9% of all kidney diseases.

We found a 3.8% prevalence of haematuria among adults in Guangzhou, which is comparable to the levels (3.5%) reported by Zhang *et al*. [8], but higher than that observed in Australia (2.0–2.5% in men and 3.0% in women) [1]. A screening study performed in Hong Kong using dipstick urinalysis from random urine samples showed an even higher prevalence of haematuria [14]. In our study, false positive results were minimized by testing all residents with morning spot haematuria dipsticks, which has been widely used in other large-scale epidemiological studies [7,8,14], and by confirmation with urine microscopic examination by an experienced technician when dipstick results were abnormal. Although repeat urine testing may help with confirmation of results and evaluation of urinary erythrocyte morphology in patients with isolated microscopic haematuria and can help distinguish between glomerular and non-glomerular disease [15], it is costly in such a large-scale screening study. About 71% of the haematuria in the present study was not associated with albuminuria or reduced eGFR, which is similar to the findings observed by Zhang *et al*. [8]. Thus, our subjects would be identified as 'normal' if haematuria was not included in the study protocol. We acknowledge that the significance of isolated microhaematuria remains controversial. Nevertheless, recent studies in Chinese patients have suggested that haematuria has important clinical implications that may identify patients at high risk for progression of renal disease [16,17]. For example, a study from Hong Kong evaluating the natural history and long-term outcome of asymptomatic and isolated haematuria documented that asymptomatic microscopic haematuria can lead to adverse renal events, thereby warranting the need for evaluation by nephrologists along with regular follow-ups [18]. IgA nephropathy, for example, may manifest as asymptomatic haematuria [19]. Another long-time follow-up study performed by mass screening of Japanese working men showed that the incidence of IgAN was as high as 143 cases per 1 million per year [20]. Because of these findings, we included examination of haematuria in our CKD screening study. However, since haematuria occurred in many females aged <45 years in our study, it may be due to early menstruation (although we purposely excluded female subjects actively menstruating) or to other non-renal causes such as bladder infections. Therefore, the importance of isolated haematuria in this population as well as separation of renal from non-renal causes will likely be revealed in long-term studies that evaluate the renal prognosis of this abnormality.

Reduced GFR is more clinically relevant to CKD and can provide more compelling evidence of CKD than does haematuria. In this study, we applied a modified MDRD equation and incorporated the Chinese CKD patient data by Ma *et al*. [10]. However, both equations have difficulties in distinguishing and classifying earlier stages of CKD. Thus, it is possible that we underestimated CKD in this population-based study based on eGFR. It will therefore be important to construct a robust and validated measure to estimate renal function in the future.

Among the risk factors related to CKD, hyperuricaemia exhibited a high OR value (OR = 1.60 for CKD and OR = 4.34 for reduced renal function, respectively) and was therefore one of the strongest risk factors. Hyperuricaemia is common in patients with CKD. However, since ours was a cross-sectional study, it was not possible to determine whether the high uric acid levels reflected the decreased GFR or whether they were etiologically linked. Some studies suggest that hyperuricaemia may be a direct pathogenic factor in CKD [21,22]; however, the effect of hyperuricaemia on progression of kidney disease in humans remains unclear [21,22]. In our study, elevated uric acid conferred a greater risk for reduced eGFR than for proteinuria, hypertension or diabetes, which is consistent with other epidemiological studies demonstrating that uric acid is a strong and independent risk factor for renal disease [23–25]. Recently, a prospective placebo-controlled trial demonstrated a significant benefit of lowering uric acid on renal function in subjects with renal impairment and asymptomatic hyperuricaemia [18]. Thus, our investigation may provide additional epidemiological evidence for a relationship between high uric acid levels and CKD. In another prospective study, the serum uric acid level was found to be an independent risk factor for adverse renal outcomes among patients with isolated microscopic haematuria [18].

In addition to classic risk factors associated with CKD, such as old age, diabetes, hypertension, cardiovascular disease and low education level, our study identified further risk factors specific to the Chinese population, which may assist in the identification of effective preventive approaches against CKD in China. For example, we found that 4.9% of the population in Guangzhou consumed potentially nephrotoxic drugs including Chinese herbs. This percentage is higher than that used by the northern Chinese of Beijing (1.8%) [8]. The reason for this difference is unknown, but may be due to a higher popularity of Chinese herbal use in adults from Guangzhou. Consistent with this finding, we noted that the long-term use of nephrotoxic medications was linked with a comparatively high OR for reduced GFR and proteinuria, which was quite different from reports in developed countries [1,2]. The nephrotoxic medications in our questionnaire included NSAIDs and herbal medicines containing aristolochic acid that is a known kidney toxin. Chinese herb nephropathy has been reported in individuals taking aristolochic acid-containing herbs such as *Aristolochia fangchi*, *A. clematits* and *A. manshuriensis* [26]. Herbal medications are widely used in China, and are especially popular among the southern populations of the country. Many herbs used for treating urinary calculi contain aristolochic acid. Due to the high prevalence of urinary calculus formation in southern China, abuse of these herbal remedies may contribute to the development of CKD. Thus, public education will be important because herbal medicines are available as over-the-counter products in many countries and a substantial number of consumers falsely believe that these products are safer than modern medicines because they are from natural sources.

We used a stratified, multistage sampling method to obtain a representative sample of the Guangzhou adult population. All participating staff were clinical doctors and medical students who received intensive training before the survey. One team worked with each community. Standardized protocols and vigorous quality control programmes were used to ensure the quality of data collection. Additional strengths include the high response rate, the fact that eGFR was calculated from the MDRD equation modified for data from Chinese CKD patients and the use of central clinical laboratories for all studied sites [10]. All of these factors guaranteed reliable data in the present study.

The current work also included several limitations. First, only one urine sample examination was obtained per patient, which made it impossible to confirm whether the haematuria or albuminuria were persistent. Previous analyses of NHANES III data demonstrated that using two urine tests to confirm kidney damage revealed a lesser prevalence of stage 1 and 2 CKD compared with using one urine test, resulting in more conservative estimates for the overall CKD prevalence (11.0 versus 14.5%) [27]. This may lead to an overestimation of CKD. As a second limitation, our data were cross-sectional and not longitudinal, which prevented determination of whether risk factors were caused by or resulted from CKD. Third, the number of populations with stage 4 and 5 CKD was rather small, which limits the power of the analysis. Finally, we were not able to elucidate the specific risk factors for haematuria in our population.

## Conclusions

This is the first epidemiological survey from a general adult population in a southern Chinese metropolis. The prevalence of CKD in Guangzhou was comparable with that in northern China and in populations from most developed countries, and was associated with a low (9.6%) awareness rate. We further identified several specific risk factors associated with CKD among southern Chinese, such as the use of herbal and other nephrotoxic medications. Such data will be of vital importance to improve our understanding of CKD and should aid in the design of health resource allocation to reduce the incidence of ESRD in China.

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*Conflict of interest statement*. None declared.

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# Prevalence of albuminuria and renal insufficiency and associated clinical factors in type 2 diabetes: the Japan Diabetes Clinical Data Management study (JDDM15)

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## Abstract

**Background.** Microalbuminuria is widely accepted as the first clinical sign of diabetic nephropathy. However, normoalbuminuric type 2 diabetic patients who have renal insufficiency (RI), i.e. low estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m$^2$, exist. We explored the prevalence of such patients and associated clinical factors.
**Methods.** We investigated the distribution of patients when stratified by albuminuria stages and chronic kidney disease (CKD) stages in a large-scale population of Japanese type 2 diabetic patients ($N = 3297$), and the common and independent factors for albuminuria and low eGFR.
**Results.** The proportion of subjects with low eGFR was 15.3% (506/3297), which was 11.4% among those with normoalbuminuria (NA) (262/2298), 14.9% among those with microalbuminuria (105/705) and 47.3% among those with macroalbuminuria (139/294). There were 262 patients with NA and low eGFR, and 63.4% of them had neither diabetic retinopathy nor neuropathy. They were older and included a higher proportion of women and patients with hypertension, hyperlipidaemia and cardiovascular disease (CVD), and fewer smokers compared with those with NA and preserved eGFR. Multiple logistic regression analysis revealed that factors commonly associated with RI and albuminuria were hypertension, CVD and proliferative retinopathy. Factors independently associated with RI were age, duration of diabetes, A1C (negative), hyperlipidaemia, smoking (negative) and macroalbuminuria, whereas those associated with albuminuria were male sex, BMI, A1C, simple retinopathy and RI.
**Conclusions.** A significant proportion of type 2 diabetic patients have normoalbuminuric RI. Renal disease in type 2 diabetes could be heterogeneous, implying the possibility of involvement of renal atherosclerosis and lipid toxicity.

**Keywords:** chronic kidney disease; glomerular filtration rate; normoalbuminuria; renal insufficiency; type 2 diabetes

## Introduction

The development of microalbuminuria has been considered to be one of the first clinical signs of a classic course of diabetic nephropathy, which leads to macroalbuminuria and then to progressive loss of glomerular filtration rate (GFR) and eventually end-stage renal disease. These steps

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