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Prevalence of and risk factors for chronic kidney disease in ten metropolitan areas of China: a cross-sectional study using three kidney damage markers

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ABSTRACT

Introduction: To estimate the up-to-date prevalence of chronic kidney disease among the health check-up population in economically developed areas of China using estimated glomerular filtration rate, urinary albumin creatinine ratio, and kidney ultrasound.

Methods: Healthcare data from 38,093 subjects in 10 megalopolises of China who had an annual health check-up in 2021 were used. The overall and stratified prevalence of chronic kidney disease by sex, age, region and comorbidity group was reported. The association between chronic kidney disease and covariates of demographics, and comorbidities were analyzed in the multivariable-adjusted logistic regression model.

Results: A total of 3837 CKD cases were detected meeting any of the three CKD diagnostic criteria, with a crude prevalence of 10.1% in the study population. Using one criterion of decreased glomerular filtration rate, albuminuria and kidney structural abnormalities alone detected 204 (5.3%), 3289 (85.7%) and 563 (14.7%) cases, respectively. The addition of kidney ultrasound detected 427 (11.1%) structural abnormality cases without decreased GFR and albuminuria. The most common abnormalities were renal masses, hydronephrosis due to obstruction and congenital anomalies of kidney and urinary tract. Female, older age, low city-tier, hypertension, diabetes, obesity, hypertriglyceridemia as well as early disease stages such as pre-hypertension, impaired fasting glucose and overweight were significantly associated with chronic kidney disease.

Conclusion: Kidney ultrasound helps to amplify the detection of CKD patients, which is a supplement to kidney function and urine protein.

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Chronic kidney disease; prevalence; risk factor; Chinese; health checkup; kidney ultrasound

1. Introduction

Chronic kidney disease (CKD) is the functional and structural damage to the kidneys resulting from a heterogeneous group of diseases [1]. In 2017, 697.5 million cases of all-stage CKD were recorded with a global prevalence of 9.1% (8.5–9.8) and the global all-age prevalence of CKD increased 29.3% since 1990 [2]. Patients with early-stage CKD can progress to end-stage renal disease (ESRD) dependent on renal replacement therapy at a different rate. CKD has continued to rise in rank among the leading causes of death worldwide because of aging and an increasing burden of risk factors for CKD including diabetes and hypertension [2]. Early detection and intervention may slow or halt disease progression to renal replacement therapy. However, the criteria for CKD diagnosis used in most epidemiologic studies were not comprehensive enough, which only included decreased estimated glomerular filtration rate (eGFR) and elevated urinary albumin to creatinine ratio (UACR) [3–7]. Renal structural abnormalities detected by imaging are one of the criteria for the definition of CKD, however, it is rarely used in adult epidemiological studies, which may lead to underdiagnosed CKD cases with normal eGFR and

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UACR. Despite the use of prenatal ultrasound screening to detect fetal anomalies, congenital anomalies of the kidney and urinary tract (CAKUT) may remain undiscovered into early adulthood. It can be detected incidentally on routine imaging of the abdomen in adulthood health checkup and is probably underdiagnosed in young adult patients [8,9]. Some anomalies such as polycystic disease, renal mass and obstructive nephropathy can be a cause of adult-onset CKD. In addition, the current prevalence of CKD in economically developed areas in China is of profound impact on public health, yet outdated and much understudied. Diabetes and hypertension, the main causes of CKD in China [10], have higher prevalences in the eastern regions of China which are more developed than the western regions [11,12]. With the acceleration of urbanization in China and the agglomeration of the population to urban metropolitan areas, understanding the prevalence of CKD in economically developed areas can help to better understand the prevalence trend in the whole country. To address the need for a more comprehensive and updated understanding of CKD prevalence, we selected 10 cities in the top metropolitan regions as well as the economic hubs of China. A health checkup database of adult urban residents was used to conduct this cross-sectional study. Since China does not build a physician referral system, the screening is mainly achieved through annual health checkup agencies. Thus, it is of great significance to understand the prevalence of CKD in the health checkup population. Improving the awareness of CKD by adding kidney ultrasound as a screening method can prove its feasibility and effectiveness in population-based settings. In addition, this study also examined the relationship between sex, age, region, city tier, and comorbidities of hypertension, dyslipidemia, obesity, diabetes, hyperuricemia and CKD prevalence to understand potential risk factors associated with this disease.

2. Methods

2.1. Study population

This was a cross-sectional study using a comprehensive Chinese healthcare database managed by Rici Healthcare Holdings Limited, China. Rici served over 3 million people in 2021 and ranked in the top three private-owned national-chained health checkup agencies in China. The population covered by health checkups comprised urban residents of pre-hired, active, and retired employees from various business clients, as well as individual walk-in visitors. This study selected 10 cities ranking in the Top 30 by GDP in 2021, including 7 representative cities (Shanghai, Suzhou, Hangzhou, Nanjing, Wuxi, Hefei, and Nantong) in the Yangtze River Delta and 3 representative cities (Shenzhen, Guangzhou and Foshan) in the Pearl River Delta. The gross domestic production (GDP) in 2021 of these two regions accounted for one-third of the country's GDP, which represents the most economically developed areas [13]. Inclusion criteria are: (1) Participated in the annual health checkup from 1 January 2021 to 31 December 2021; (2) Lived in selected cities in the Yangtze River Delta or the Pearl River Delta; (3) Had test results of serum creatine (SCr), UACR, and renal ultrasound examination. Exclusion criteria are: (1) Aged younger than 18 years old; (2) Had incomplete medical records. A total of 38,096 samples were included that were randomly selected from 10 cities according to the proportion of the number of people who participated in the health checkups in each city. Three subjects were excluded for incomplete medical records and 38,093 samples were analyzed (Figure 1). Approval for this research was obtained by the ethical review committee of Rici Health Care. Informed consent of each subject was not required because this study used only deidentified data.

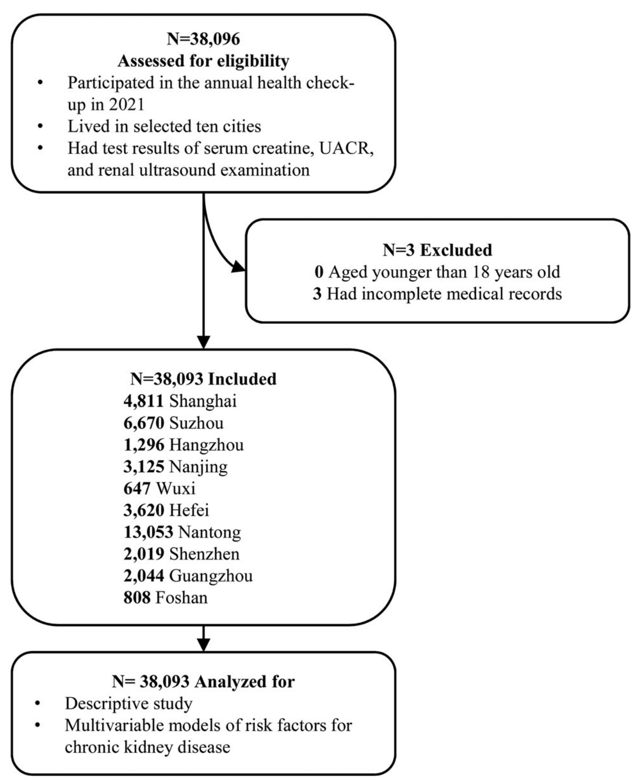

Figure 1. Flow diagram of the subjects in this study. UACR: urinary albumin to creatinine ratio.

2.2. Definition of chronic kidney disease

CKD is defined by meeting any of the following kidney damage markers: (1) calculated eGFR using the CKD-EPI creatine equation <60 mL/min per 1.73 m^2; (2) UACR ≥30 mg/g or ≥3 mg/mmol; (3) Renal structural abnormalities detected by ultrasound (polycystic kidney, dysplastic kidney, obstructive hydronephrosis, renal mass or infiltrative disease causing renal enlargement, small and hyperechoic kidneys, post-nephrectomy or partial nephrectomy, history of kidney transplantation) [14]. The blood and urine specimens were collected in the morning at each clinic in a fasting status. The one-time SCr and spot UACR were examined at the medical laboratory in each city. Quantitative albuminuria was measured with immunoturbidimetric tests. Blood and urinary creatinine were measured with an enzymatic method. UACR was calculated by dividing urine albumin by creatinine. All the study laboratories completed standardization and certification programs. The serum creatinine assays used a calibration method traceable to a NIST SRM 967 L1& L2 reference standard and the urine creatinine assays to a NIST SRM 3667. The urine albumin assays used calibrator and value provided in the kit. The calibrator is traceable to a primary standard which is prepared gravimetrically using reagent grade human serum albumin. Measurements of SCr were used directly for calculation of eGFR with CKD-EPI equation [15]. Validation studies on CKD-EPI equation in the Chinese population confirmed its better performance in predicting of eGFR than other equations [16,17]. It was recommended to use to calculate eGFR by the guidelines for early screening of CKD in China [18]. Renal masses are specific imaging findings when using ultrasound technique, for example, solid nature, internal characteristics of septa and calcifications, well-defined or infiltrative margin [19]. Hydronephrosis is defined as dilatation of the drainage system of the kidney, i.e. the calices, the infundibula, and the renal pelvis [20]. It can be due to obstructive causes of ureteric stone, renal tumor, abnormal rotation of kidney, tumor compressing urinary tract etc. The spectrum of CAKUT is broad and consists of a series of diseases [21]. Standard protocol of Chinese Guidelines for Abdominal Ultrasound Examination was followed in the kidney ultrasound scan [22].

2.3. Demographic and other covariates

Sex, age, and resident city of each participant was collected from the client information. The city-tier was classified into three levels of Tier-1, Tier-2 and Tier-3 mainly based on gross domestic product per capita and urban population. Tier-1 represented the most economically developed areas. Past medical history of hypertension, diabetes, and hyperuricemia was ascertained by a positive response to the following question by trained physicians: "Has a doctor ever told you that you have hypertension, diabetes, gout or hyperuricemia?" Blood pressure was measured twice at 5-min intervals using Omron HBP-9020 digital sphygmomanometer. The mean of the two readings was used Hypertension was defined as a systolic blood pressure (SBP) ≥140 mmHg, or a diastolic blood pressure (DBP) ≥90 mmHg, and/or a self-reported history of physician-diagnosed hypertension [23]. Height and weight were measured by a Woshen WS-H300 automatic digital physician scale. Body mass index (BMI) was calculated as weight in kilograms (kg) divided by square of height in meters (m^2) and was categorized as normal (<24.0 kg/m^2), overweight (24.0-27.9 kg/m^2), and obese (> 28.0 kg/m^2) as per the guidelines of the Chinese population [24]. Fasting blood glucose (FBG), hemoglobin A1c (HbA1c), serum total cholesterol (TC), triglycerides (TG), serum creatine and serum urate were tested in a fasting state. Diabetes was defined as FBG ≥7.0 mmol/L, or HbA1c ≥ 6.5%, and/or a self-reported history of diabetes [25]. TC level was categorized as normal (< 5.2 mmol/L), borderline elevated (5.2–6.2 mmol/L), and hypercholesterolemia (≥6.2 mmol/L). TG level was categorized as normal (<1.7 mmol/L), borderline elevated (1.7–2.3 mmol/L), and hypertriglyceridemia (≥2.3 mmol/L) [26]. Hyperuricemia was defined as serum urate ≥420 mmol/L and/or a self-reported history of gout or hyperuricemia [15]. All data were recorded in the electronic health record system.

2.4. Statistical analyses

The crude prevalence of CKD was reported in the study population, and the stratified prevalence was reported by sex, age, region, city, and comorbidities. The prevalence calculated by three markers of kidney function was reported by disease stage. The diseases and case numbers of structural abnormalities detected by kidney ultrasound was described. Multivariate logistic regression model was used to investigate the associations between demographic, comorbidity factors, and CKD adjusting for sex, age, region, city-tier, hypertension, diabetes, triglyceride level, total cholesterol level, obesity, and hyperuricemia. The results were reported as odds ratios with 95% confidence intervals. Stata 16 (StataCorp, College Station, TX) was used for all analyses.

3. Results

3.1. Prevalence of CKD

A total of 38,093 subjects with complete health checkup records were included in the study, among which 3837 CKD cases (1,995 women and 1,842 men) were detected by any of the three kidney damage markers in this study as aforementioned. The overall CKD prevalence was 10.1% in the study population, with a higher prevalence in females than that in males (11.7% *vs* 8.7%). Among the CKD patients, 204 (0.5%) cases had decreased eGFR, 3289 (8.6%) cases had elevated UACR, and 563 cases (1.5%) cases were detected with kidney structural abnormalities. The age group was divided into 7 subgroups by every 10 years old. The prevalence of CKD increased with age, as the highest prevalence of CKD of 38.8% was found in the subgroup over 80 years old. Among three kidney damage markers, the positive rate of decreased GFR and proteinuria all increased with age, but the positive rate of renal structural abnormalities showed subtle changes among age groups. The crude prevalence of CKD in the Yangtze river delta was higher than that in the Pearl river delta (10.6% *vs* 6.3%). The CKD prevalence stratified by the city was from the lowest in Shanghai (4.6%) to the highest in Nantong (14.4%) (Appendix 1). Among the metabolic diseases investigated, the prevalence of top three metabolic diseases commonly associated with CKD in this population were diabetes (25.1%), hypertension (21.4%), and obesity (16.0%) (Table 1).

3.2. Markers of kidney damage

Among the 3289 CKD patients who had proteinuria, 83 (2.5%) had decreased eGFR, and 124 (3.8%) had renal structural abnormalities. Of the 563 CKD patients who had renal structural abnormalities, 26 (4.6%) had decreased eGFR (Table 2). There were 14 (0.4%) CKD patients detected by all three kidney damage markers at the same time, and meanwhile, there were 3632 (94.7%) CKD patients detected by a single indicator (Figure 2). We note that the yellow area represents the CKD patients omitted by previous diagnosis while our study of CKD prevalence was able to include them in the analysis. Table 3 shows the number and percentage of renal structural abnormalities detected by kidney ultrasound. The top three diseases found are 265 (47.1%) cases of renal mass, 159 (28.2%) cases of obstructive hydronephrosis, and 51 (9.1%) cases of congenital anomalies of kidney and urinary tract.

3.3. Risk factors associated with CKD prevalence

After adjustment for sex, age, region, city tier, and all comorbidities, women were found to have almost 2-fold higher odds of having CKD than men (adjusted OR [aOR] = 1.95 [95% CI = 1.81–2.12]). Accordingly, the odds of having CKD increased with age, with the highest odds in the subgroup of over 80 years old compared to 18–29 years old group (aOR = 7.67 [95% CI = 4.80–12.25]). Subjects who lived in the Yangtze River Delta had similar odds of having CKD than those in the Pearl River Delta (aOR = 1.15 [95%CI = 0.99–1.34]). Subjects who lived in the less economically developed Tier-3 cities had higher odds of having CKD than those in well-developed Tier-1 cities (aOR = 2.54 [95%CI = 2.33–2.90]). Compared with the healthy subjects, the subjects with hypertension, diabetes, obesity, hypertriglyceridemia, and hyperuricemia had higher odds of having CKD, with aOR (95% CI) of 3.38 (3.02–3.79), 2.36 (2.13–2.62), 1.56 (1.41–1.74), 1.45 (1.32–1.59) and 1.37 (1.23–1.51) respectively. In contrast, hypercholesterolemia subjects had similar odds of having CKD to normal cholesterol level subjects (aOR = 1.04 [95% CI = 0.93–1.16]) (Table 4).

4. Discussion

This study used a health checkup database of Chinese population in 10 economically developed cities in the Yangtze river delta and Pearl river delta. We found an overall CKD prevalence of 10.1% in the study population. We used three kidney damage markers to assess the CKD prevalence and found kidney ultrasound was feasible in population-based settings. This addition in CKD diagnosis can identify more patients even without a decreased eGFR or increased UACR, leading to a more accurate prevalence estimate. Considering kidney ultrasound is accessible and less expensive in China, it can be used as a supplement method to improve the diagnosis accuracy and amplify the detection of CKD patients. This study conducted an epidemiological survey of urban residents in the largest urban agglomerations of China. These areas are characterized by high urbanization level, population density, and economic development, which depicts the developmental trend of regional-level urban agglomerations with various changes in nutrition intake and lifestyle factors. The CKD prevalence in this study is higher than the urban prevalence reported in 2018 (7.9%) [4] as well as the Tier-3 urban prevalence reported in 2009–2010 (6.3%) [3]. It may attribute to the increasing incidence of diabetes, hypertension, and study population selection. In addition, multivariate logistic regression analysis

Table 1. Characteristics of participants according to markers of kidney damage in the analysis samples.

	Total	Participants with eGFR <60 mL/min per 1.73 m^2	Participants with albuminuria[b]	Participants with structural abnormalities[c]	Participants with any of three markers of kidney damage
Total[a]	38,093 (100)	204 (0.5)	3289 (8.6)	563 (1.5)	3837 (10.1)
Men	21,091 (55.4)	141 (69.1)	1559 (47.4)	267 (47.4)	1842 (48)
Age, years					
18–29	3910 (10.3)	0 (0)	137 (4.2)	17 (3)	151 (3.9)
30–39	10020 (26.3)	5 (2.5)	495 (15.1)	115 (20.4)	595 (15.5)
40–49	8566 (22.5)	17 (8.3)	618 (18.8)	116 (20.6)	714 (18.6)
50–59	10,123 (26.6)	47 (23)	1166 (35.5)	186 (33)	1339 (34.9)
60–69	4407 (11.6)	56 (27.5)	627 (19.1)	95 (16.9)	718 (18.7)
70–79	964 (2.5)	59 (28.9)	221 (6.7)	32 (5.7)	280 (7.3)
≥80	103 (0.3)	20 (9.8)	25 (0.8)	2 (0.4)	40 (1)
Region[d]					
Yangtze river delta	33,222 (87.2)	169 (82.8)	3104 (94.4)	460 (81.7)	3532 (92.1)
Pearl river delta	4871 (12.8)	35 (17.2)	185 (5.6)	103 (18.3)	305 (7.9)
Systolic BP, mmHg	124.1(17.9)	141.4 (23.1)	137.3 (20.8)	128.0 (19.9)	135.9 (20.9)
Diastolic BP, mmHg	75.4 (11.8)	80.8 (14.3)	82.0 (13.0)	76.5 (12.3)	81.1 (13.0)
Triglyceride, mmol/L	1.2 (0.8, 1.9)	1.5 (1.1, 2.4)	1.4 (1.0, 2.4)	1.2 (0.9, 1.9)	1.4 (1.0, 2.3)
Body-mass index, kg/m^2	24.4 (3.5)	25.5 (3.4)	25.6 (3.7)	24.7 (3.5)	25.5 (3.7)
Total cholesterol, mmol/L	5.0 (1.0)	5.0 (1.0)	5.2 (1.0)	5.1 (1.0)	5.2 (1.0)
Fasting blood glucose, mmol/L	5.4 (1.3)	6.0 (2.0)	6.1 (2.3)	5.5 (1.3)	6.0 (2.2)
Hemoglobin A1C, %	5.6 (0.8)	6.0 (1.3)	6.0 (1.4)	5.6 (0.9)	6.0 (1.3)
Uric acid, μmol/L	329.1 (94.1)	447.4 (114.2)	328.6 (100.0)	331.6 (102.1)	331.9 (102.3)
Serum creatinine, μmol/L	66.9 (16.1)	133.8 (71.7)	65.9 (24.0)	71.0 (29.0)	67.7 (27.2)
eGFR, mL/min per 1.73 m^2	108.0 (16.4)	49.4 (11.2)	103.0 (18.4)	99.7 (21.1)	101.5 (20.0)
UACR, mg/g	8.9 (5.7, 16.1)	31.8 (9.8, 262.8)	53.85 (37.7, 100.9)	13.45 (7, 39.6)	49.1 (34.7, 92.9)
Comorbidities					
Hypertension	8220 (21.6)	113 (55.4)	1585 (48.2)	170 (30.2)	1760 (45.9)
Hypertriglyceridemia	6477 (17.0)	58 (28.4)	858 (26.1)	88 (15.6)	946 (24.7)
Obesity	5604 (14.7)	45 (22.1)	806 (24.5)	93 (16.5)	894 (23.3)
Hypercholesterolemia	4132 (10.8)	24 (11.8)	487 (14.8)	70 (12.4)	546 (14.2)
Diabetes	2902 (7.6)	50 (24.5)	672 (20.4)	59 (10.5)	727 (18.9)
Hyperuricemia	6352 (16.7)	110 (53.9)	596 (18.1)	104 (18.5)	729 (19)

BP: blood pressure; eGFR: estimated glomerular filtration rate; UACR: urinary albumin to creatinine ratio.
[a]Data are presented as *n* (%) or mean (SD) unless stated otherwise. Triglyceride and UACR are presented as median (IQR) because of skewed data.
[b]Albuminuria is defined as urine albumin creatine ratio ≥30 mg/g or ≥3 mg/mmol.
[c]Structural abnormalities were detected by kidney ultrasound.
[d]Yangtze river delta includes seven cities of Shanghai, Suzhou, Hangzhou, Nanjing, Wuxi, Nantong, Hefei. Pearl river delta includes three cities of Guangzhou, Shenzhen and Foshan.

Table 2. Prevalence of markers of kidney function by disease stage in the analysis samples.

		Kidney function		Albuminuria[a]		Structural abnormalities[b]		
Stage	eGFR (mL/min per 1.73 m^2)	n	Prevalence % (95% CI)	n	Prevalence % (95% CI)	n	Prevalence % (95% CI)	CKD[c] prevalence (95% CI)
1	≥90	33125	87.0 (86.6–87.3)	2666	8.0 (7.8–8.3)	409	1.2 (1.1–1.4)	9.1 (8.8–9.4)
2	60-89	4764	12.5 (12.2–12.8)	540	11.3 (10.5–12.3)	128	2.7 (2.3–3.2)	13.2 (12.3–14.2)
3	30-59	187	0.49 (0.41–0.59)	68	36.4 (29.7–43.5)	23	12.3 (8.3–17.9)	100
3a	45-59	157	0.41 (0.35–0.48)	48	30.6 (23.8–38.3)	12	7.6 (4.4–13.0)	100
3 b	30-44	30	0.079 (0.055–0.11)	20	66.7 (47.5–81.5)	11	36.7 (21.1–55.7)	100
4	15-29	13	0.034 (0.020–0.059)	12	92.3 (55.4–99.1)	2	15.4 (3.3–49.3)	100
5	<15	4	0.011 (0.004–0.028)	3	75 (70.7–99.2)	1	25 (0.84–92.9)	100
Total		38,093		3289	8.6 (8.4–8.9)	563	1.5 (1.4–1.6)	

eGFR: estimated glomerular filtration rate; 95% CI: 95% confidence interval; CKD: chronic kidney disease.
[a]Albuminuria is defined as urine albumin creatine ratio ≥30 mg/g or ≥3 mg/mmol.
[b]Structural abnormalities were detected by kidney ultrasound.
[c]CKD was defined as eGFR <60 mL/min per 1.73 m^2 or albuminuria or structural abnormalities.

showed that not only hypertension, diabetes, and obesity had a positive association with CKD, but also early stages of the metabolic disease, such as prehypertension, impaired fasting blood glucose, and overweight are significantly associated with CKD.

CKD is defined as functional abnormalities or structural abnormalities lasting for more than 3 months as per "Kidney Disease: Improving Global Outcomes" (KDIGO) guideline [14]. The diagnostic criteria include decreased glomerular filtration rate, albuminuria,

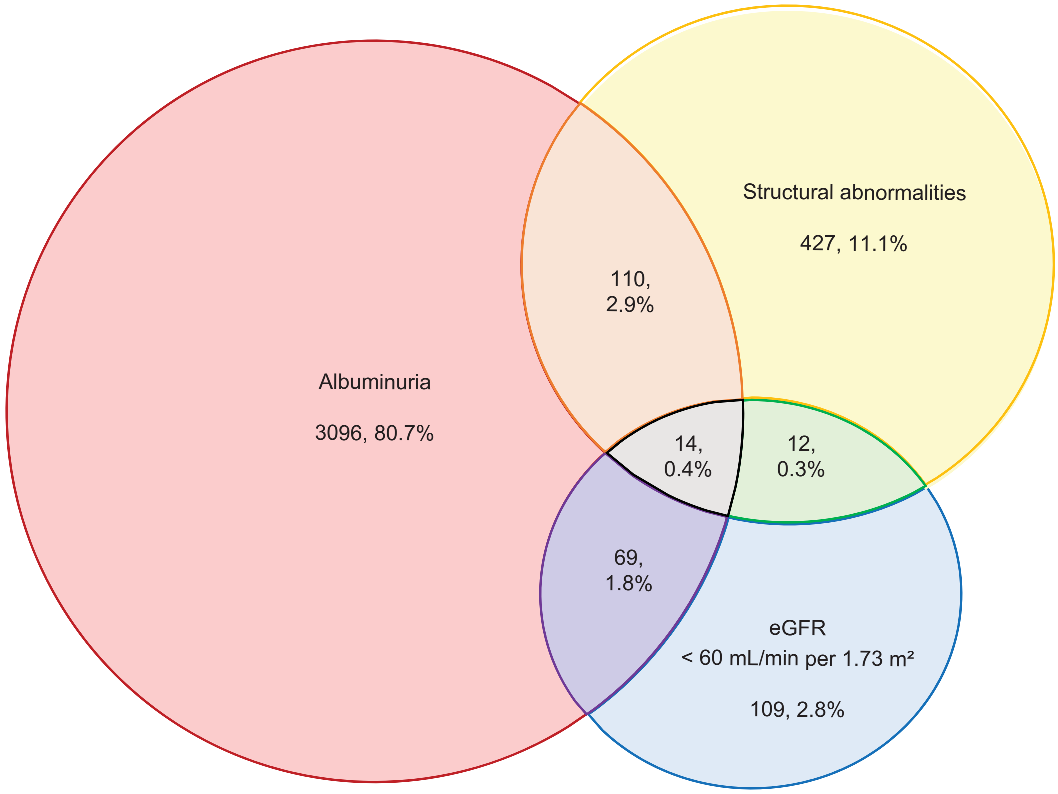

Figure 2. Case number detected by three kidney damage markers in 3837 chronic kidney disease patients. The red shape represents patients with albuminuria, which is defined as urine albumin creatine ratio $\geq$30 mg/g or $\geq$3 mg/mmol. The yellow represents patients with structural abnormalities detected by kidney ultrasound. The blue shape represents patients with decreased eGFR. The overlapping shapes represent patients detected by more than one kidney damage marker. The orange, green and purple shape represents patients detected by two diagnostic methods and the grey shape is by all three diagnostic methods. The percentage in each shape is calculated by dividing 3837 chronic kidney disease patients by case number in the corresponding shape.

Table 3. Disease spectrum of structural abnormalities by kidney ultrasound among 563 participants.

	n (%)
Renal masses	265 (47.1)
Hydronephrosis due to obstruction	159 (28.2)
CAKUT	51 (9.1)
Solitary kidney	24 (4.3)
Duplex kidney or duplex collecting system	15 (2.7)
Ectopic kidney	8 (1.4)
Fusion kidney	3 (0.5)
Dysplastic kidneys	1 (0.2)
Small and hyperechoic kidneys	31 (5.5)
History of nephrectomy or partial nephrectomy	22 (3.9)
Polycystic kidneys	16 (2.8)
Medullary sponge kidney	10 (1.8)
Diminished corticomedullary differentiation	7 (1.2)
Autonephrectomy	1 (0.2)
History of kidney transplantation	1 (0.2)

CAKUT: Congenital anomalies of kidney and urinary tract. If the participant meets two imaging structural abnormalities of CKD at the same time, the first diagnosis by ultrasound shall prevail.

urinary sediment abnormalities, renal tubular disorders, pathologic abnormalities, structural abnormalities detected by imaging, and a history of kidney transplantation. The epidemiological investigations usually use one-time measured serum creatinine value to calculate eGFR as well as one-time spot UACR as the diagnosis criteria of CKD [3,4,27,28]. But eGFR can be normal in the early stage of glomerular disease, vascular disease, and unilateral kidney involvement with a compensated kidney on the other side. This study found 2666/3289 (81.1%) albuminuria patients and 409/563 (72.6%) structural abnormalities patients had normal eGFR. UACR has a greater significance in detecting glomerular diseases and vascular diseases, and has a low positive rate for tubulointerstitial diseases, cystic kidney diseases, and congenital structural abnormalities. Some CKD prevalence studies used hematuria as an additional criterion for CKD [6,7]. But microscopic hematuria diagnosed by dry chemistry or microscopic examination had a high false-positive rate [29]. Dysmorphism of urinary red blood cells was necessary to identify a renal source of hematuria. Otherwise, it may lead to an overestimation of the prevalence of CKD. Thus, this study retained decreased eGFR and albuminuria detected by UACR as the diagnostic criteria. In addition, it added third diagnostic criteria of structural abnormalities detected by kidney ultrasound for CKD, aiming to improve the positive rate of CKD

Table 4. Multivariable models of risk factors for chronic kidney disease among 38,093 participants in China, 2021.

	Participants with CKD, *n* (%)	Unadjusted odds	Fully-adjusted odds ratio (95% CI)[a]
Sex			
Men	1842 (8.7)	0.096	Reference
Women	1995 (11.7)	0.130	1.95 (1.81–2.12)
Age, years			
18–29	151 (3.9)	0.040	Reference
30–39	595 (5.9)	0.063	1.32 (1.10–1.59)
40–49	714 (8.3)	0.091	1.54 (1.28–1.85)
50–59	1339 (13.2)	0.150	2.07 (1.73–2.47)
60–69	718 (16.3)	0.190	2.35 (1.94–2.85)
70–79	280 (29.1)	0.410	4.30 (3.42–5.41)
≥80	40 (38.8)	0.630	7.67 (4.80–12.25)
Region			
Yangtze river delta	3532 (10.6)	0.120	Reference
Pearl river delta	305 (6.3)	0.067	1.15 (0.99–1.34)
City–tier[b]			
Tier–1	478 (5.4)	0.057	Reference
Tier–2	1479 (9.2)	0.100	1.81 (1.59–2.06)
Tier–3	1880 (14.4)	0.170	2.54 (2.23–2.90)
Comorbidities			
Hypertension			
No	2076 (7.0)	0.075	Reference
Prehypertension[c]	1113 (18.2)	0.220	1.94 (1.78–2.12)
Yes	648 (30.5)	0.440	3.38 (3.02–3.79)
Diabetes			
No	2814 (8.5)	0.093	Reference
IFG[d]	296 (15.1)	0.180	1.41 (1.23–1.62)
Yes	727 (25.1)	0.330	2.36 (2.13–2.62)
Triglyceride level, mmol/L			
Normal	2286 (8.7)	0.095	Reference
1.7–2.3	605 (11.3)	0.130	1.11 (1.00–1.23)
≥ 2.3	946 (14.6)	0.170	1.45 (1.32–1.59)
Total cholesterol level, mmol/L			
< 5.2	2112 (9.1)	0.100	Reference
5.2–6.2	1179 (10.9)	0.120	1.00 (0.92–1.08)
≥ 6.2	546 (13.2)	0.150	1.04 (0.93–1.16)
Obesity			
No	1332 (7.5)	0.081	Reference
Overweight	1611 (11.0)	0.120	1.17 (1.07–1.27)
Obese	894 (16.0)	0.190	1.56 (1.41–1.74)
Hyperuricemia			
No	3108 (9.8)	0.110	Reference
Yes	729 (11.5)	0.130	1.37 (1.23–1.51)

CKD: chronic kidney disease; 95% CI: 95% confidence interval; IFG: impaired fasting glucose.
[a]Fully adjusted odds ratio was adjusted for sex, age, region, city tier and all the other comorbidities. The widths of the confidence intervals were adjusted for multiple comparisons.
[b]The cities in the subgroup of Tier-1 include Beijing, Shanghai, Guangzhou and Shenzhen. The cities in the subgroup of Tier-2 include Hangzhou, Suzhou, Nanjing, Hefei and Foshan. The city in the subgroup of Tier-3 includes Nantong. Tier-1 represents the most economically developed areas.
[c]Pre-hypertension was defined as SBP between 120–139 mmHg, or a DBP between 80–89 mmHg.
[d]IFG was defined as fasting blood glucose between 6.1–7.0 mmol/L.

caused by kidney mass, cystic disease, and congenital abnormalities. This study showed that 427/563 (75.8%) structural abnormality cases without decreased GFR and albuminuria were detected by kidney ultrasound, accounting for 11.1% of all CKD cases (Figure 2). The result suggested that kidney ultrasound is a feasible supplement to kidney function and urine protein, helping to improve the detection of CKD in epidemiological investigations. The most common abnormalities detected by ultrasound were renal masses, hydronephrosis due to obstruction, and CAKUT. Most of the renal masses are suspected of hamartomas. Complex cysts and solid masses are also common. We notice the diagnosis of renal hamartomas based on renal ultrasonography alone is not definite. Actually, the indication of angiomyolipoma under sonogram may be diagnosed as angiomyolipoma, renal cell carcinoma, calculus and normal variants under computed tomography or surgical pathology [30]. The prevalence of CAKUT for children under 14 years old in Beijing, China was reported as 1.67% by ultrasound screening [31]. CAKUT is probably underdiagnosed in young adult patients and this study reported 51 (0.1%) cases in the study population.

This study also investigated the relationship between gender, age, city tier, comorbidities and CKD by multivariate logistic regression analysis. The result suggested that female gender, older age, and low-city tier may increase the risk of developing CKD. The prevalence of CKD in women is generally higher than that in men in various countries in the research on the global burden of disease [32]. The gender difference in CKD may be related to the gender difference in the prevalence of primary disease and the availability of medical resources [33]. The findings in this study showed similar gender differences that women had higher odds of having CKD than men (aOR = 1.95 [95% CI = 1.81–2.12]). The global prevalence of CKD has increased by 29.3% from 1990 to 2017, mainly from countries with low and medium sociodemographic index (SDI). The countries with high SDI have a low prevalence of CKD than those with low SDI (6.8% *vs* 9.2%) [2]. The trend was alike in China where the prevalence of CKD in urban residents is lower than that in rural residents (7.9% *vs* 8.6%) [4]. This study showed that the relative risk of having CKD among residents in Tier-2 cities and Tier-3 cities is 1.81-times and 2.54-times that of residents in well-developed Tier-1 cities, respectively. The result was consistent with the above-mentioned literatures, suggesting that effective intervention of metabolic diseases such as hypertension and diabetes can reduce the occurrence of CKD. The association between CKD and comorbidities of hypertension, diabetes, obesity, hyperuricemia, and dyslipidemia has been affirmed [1]. Among these comorbidities, our study showed that hypertensive patients (aOR = 3.38 [3.02–3.79]) had the highest relative risk of developing CKD, even those with prehypertension had a higher relative risk than normal subjects (aOR = 1.94 [95% CI= 1.78–2.12]). Similarly, impaired fasting glucose patients (aOR = 1.41 [95% CI= 1.23–1.62]) had an increased risk of developing CKD compared to normal individuals, and overweight patients (aOR = 1.17 [95% CI= 1.07–1.27]) had a higher risk of developing CKD than normal participants. Intervention in the early stage of metabolic diseases may halt or delay the occurrence of CKD.

This study was based on a large healthcare database covering 10 cities to estimate the current prevalence of CKD among urban residents in economically developed areas of China. The health checkup population is a group of people dedicated to disease prevention in public health. Raising awareness of CKD in healthy asymptomatic populations is of great significance and importance. This study also has several limitations. First, CKD is more epidemic among women and old-aged adults, but 55.4% of the studied population were men and around 75% were aged from 30 to 59 years old. In addition, the population receiving annual health-check in commercial institutions might be with high levels of socioeconomic status. The population bias of this study very likely underestimated the prevalence in the general population. Second, this study didn't use CKD-EPI equation without the specification of race to calculate eGFR [34]. The new CKD-EPI equation didn't have any performance validation study in Chinese population by far. Third, CKD was defined by one-time serum creatinine and spot UACR test results. Unconfirmed kidney function damage persisting for more than 3 months may overestimate the prevalence of CKD, especially given this is a fairly young population and so transient proteinuria likely common. Kidney ultrasound may have inter-operator variability and not be as a solid definition as under computed tomography or surgical pathology. Fourth, information on ethnicity, smoking, and nephrotoxic drug use was not available in the health checkup database. These factors have been documented in the literature to affect the prevalence of CKD [1]. Finally, this cross-sectional study cannot reflect the prevalence trend in China, and further studies on CKD prevalence changes over a longer period would be helpful to answer this question.

5. Conclusion

This study uses the largest sample size to investigate the prevalence of CKD in the Chinese health checkup population. Kidney ultrasound can help to detect CKD patients with normal eGFR and UACR. It can be used as one of the routine methods for CKD epidemiological surveys. Female gender, older age, low city tier, hypertension, diabetes, obesity, hypertriglyceridemia, and hyperuricemia have a positive association with CKD. Early stages of the metabolic disease, such as prehypertension, impaired fasting blood glucose, and being overweight may also increase the risk of developing CKD.

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Authors' contributions

YJW conceptualized the study. ZJL and XYQ designed the study and suggested the statistical method. WYL and ZHY took responsibility for the integrity of the data. FTX and WXX performed the data analysis. FTX wrote the first and subsequent drafts of the manuscript. ZBL and ZL provided administrative support. YJW and LYS supervised this study. All authors critically revised the manuscript for intellectual content and approved the final draft for submission.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Appendix 1. Crude city prevalence of chronic kidney disease by markers of kidney damage in the analysis sample. [a]

	Total	Participants with eGFR <60 mL/min per 1.73 m^2	Participants with albuminuria[b]	Participants with structural abnormalities[c]	Participants with any of three markers of kidney damage
Total	38, 093 (100)	204 (0.5)	3289 (8.6)	563 (1.5)	3837 (10.1)
Shanghai	4811 (12.6)	30 (14.7)	143 (4.3)	64 (11.4)	219 (5.7)
Suzhou	6670 (17.5)	35 (17.2)	589 (17.9)	104 (18.5)	674 (17.6)
Hangzhou	1296 (3.4)	8 (3.9)	74 (2.2)	14 (2.5)	89 (2.3)
Nanjing	3125 (8.2)	16 (7.8)	340 (10.3)	46 (8.2)	378 (9.9)
Wuxi	647 (1.7)	2 (1)	67 (2)	2 (0.4)	70 (1.8)
Hefei	3620 (9.5)	20 (9.8)	159 (4.8)	59 (10.5)	222 (5.8)
Nantong	13, 053 (34.3)	58 (28.4)	1732 (52.7)	171 (30.4)	1880 (49)
Shenzhen	2019 (5.3)	18 (8.8)	95 (2.9)	42 (7.5)	149 (3.9)
Guangzhou	2044 (5.4)	8 (3.9)	59 (1.8)	52 (9.2)	110 (2.9)
Foshan	808 (2.1)	9 (4.4)	31 (0.9)	9 (1.6)	46 (1.2)

eGFR: estimated glomerular filtration rate.
[a]Data are *n*(%).
[b]Albuminuria is defined as urine albumin creatine ratio $\geq$30 mg/g or $\geq$3 mg/mmol.
[c]Structural abnormalities were detected by kidney ultrasound.