ORIGINAL ARTICLE

Chronic kidney disease in Chinese postmenopausal women: A cross-sectional survey

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Abstract

Introduction: Despite advances in the management of chronic kidney disease (CKD), there is ongoing uncertainty regarding the prevalence of CKD in postmenopausal women. This study was designed to investigate both CKD prevalence and related risk factors in a cohort of postmenopausal Chinese women.

Materials and Methods: A cross-sectional survey was administered to a nationally representative sample of female Chinese participants, including a total of 47,204 subjects, among whom were 8573 self-reported postmenopausal women. CKD was defined as either an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2 body surface area or else the presence of albuminuria. All subjects completed a questionnaire that included items related to their lifestyles and medical histories. Data were collected on blood pressure, serum creatinine, urinary albumin, and urinary creatinine. Risk factors correlated with the presence of CKD were analyzed using logistic regression analysis.

Results: Results showed that the adjusted prevalence of an eGFR of < 60 mL/min/1.73 m^2 among this postmenopausal survey cohort was 5.3% (95% confidence interval: 4.7–6.1) and of albuminuria, 12.4% (11.7–13.1). The overall prevalence of CKD in this postmenopausal cohort was 16.6% (15.8–17.4). Factors associated with kidney pathology included nephrotoxic drug use, history of cardiovascular disease, hyperuricemia, hypertension, and diabetes (the lower limit of multivariable adjusted odds ratios > 1).

Conclusion: The current study revealed a high prevalence of CKD in Chinese postmenopausal women. These results provide baseline data for disease prevention and treatment.

Key words: Albuminuria, Chinese postmenopausal women, chronic kidney disease, creatinine, cross-sectional survey, glomerular filtration rate

Date of Acceptance: 11-Jul-2016

Introduction

Emerging lines of evidence demonstrate that perimenopausal women (defined as the time period immediately prior to and 5 years following menopause onset) have a high risk of developing chronic kidney disease (CKD).[1,2] Nevertheless, CKD and its associated risk factors in postmenopausal women in China are still poorly understood. In the present study, a cross-sectional survey of a nationally representative sample of adult Chinese females was conducted. The association between CKD and postmenopausal status was studied, and this study revealed several factors related to kidney damage in postmenopausal women.

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Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/1119-3077.198314

How to cite this article: Pei F, Zhou Z, Li Y, Ren Y, Yang X, Liu G, *et al*. Chronic kidney disease in Chinese postmenopausal women: A cross-sectional survey. Niger J Clin Pract 2017;20:153-7.

Materials and Methods

Study participants

A multistage, stratified sampling method was used, as previously described in detail.[3] Briefly, participants from 13 provinces located in different geographical regions of China including east, south, middle, north, northwest, and southwest were included in this study cohort. Urban and rural districts were then selected from each included province. A total of 50,550 individuals were invited to participate, among whom 47,204 completed the survey. From this survey population, 8573 postmenopausal women were recruited for further analysis that formed the basis for this study. Postmenopause was defined as a self-reported physiological condition. The study was approved by the Ethics Committee of our university. All participants provided written informed consent prior to data collection.

Screening protocol

Data were collected in examination centers located within local health stations or community clinics within participants' residential areas. These on-site screenings were performed between September 2009 and September 2010. With the assistance of trained general practitioners, medical students, and nurses, all participants completed a questionnaire documenting socio-demographic status (e.g age and education), lifestyle (e.g smoking and drinking habits), and personal and family health history (e.g hypertension, diabetes, and kidney disease). Anthropometric measurements, including weight and height, were also collected. All study investigators received training that taught the methods and processes utilized in the study.

Evaluation of renal injury indicators and other covariates

Participants' blood and urine samples were analyzed at a central laboratory located within each province. Urinary albumin and creatinine were measured, albuminuria by means of immunoturbidimetric tests and creatinine by Jaffe's kinetic method.[4] The urinary albumin to creatinine ratio (ACR; mg albumin/g creatinine) was calculated. Albuminuria was defined as an ACR >30 mg/g. Blood samples were collected by venipuncture, and serum creatinine was measured by the same method employed for urinary creatinine detection. Estimated glomerular filtration rate (eGFR) was calculated using the following equation as previously reported:[5]

$$\text{eGFR (mL/min/1.73 m}^2\text{)} = 175 \times \text{SCr}^{-1.234} \times \text{age}^{-0.179} \times 0.79$$

Where, SCr stands for serum creatinine (mg/dL).

CKD was defined as an eGFR <60 mL/min/1.73 m^2 or the presence of albuminuria, as defined above.

CKD was Staged 1 through 5, according to the kidney disease outcome quality initiative,[6] and Stage 3 CKD was further sub-categorized as either Stage 3a (≥45 mL/min/1.73 m^2) or 3b (<45 mL/min/1.73 m^2).

Resting blood pressure was measured using a sphygmomanometer. The average of the three readings was calculated, unless the difference between readings was higher than 10 mm Hg, in which case, the average of the two closest measurements was calculated. Hypertension was defined as follows: Either a systolic blood pressure ≥140 mm Hg or a diastolic blood pressure ≥90 mm Hg or the use of antihypertensive drugs in the 2 weeks preceding the study onset, irrespective of blood pressure measurements or any self-reported history of hypertension. Fasting blood glucose was measured enzymatically by a glucose oxidase assay. Diabetes was defined as either a fasting plasma glucose level ≥7.0 mM, or by the patient's use of hypoglycemic agents regardless of fasting plasma glucose, or by a self-reported history of diabetes. Total serum lipid measurements included low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides; these and serum uric acid were measured with commercially available reagents. The provincial testing laboratories used a timed-endpoint colorimetric method to measure LDL-C and HDL-C. Hyperuricemia was defined as a plasma uric acid concentration >363 μM.

Statistical analysis

EpiData software (freeware, version 3.1; EpiData Association, www.EpiData.dk) was utilized for data input and management. Analyses were performed with SUDAAN (version 10, RTI International, SUDAAN@rti.org) and SAS (version 9.1, SAS Institute Inc., Cary, NC, USA). Normally distributed data are presented as proportions for categorical variables or as mean ± standard deviation (SD) for continuous variables (e.g age). ACR is presented as median (interquartile range).

The association between self-reported postmenopausal status and the presence of CKD was studied by means of logistic regression models. Crude and multivariable adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Covariates in the multivariable logistic regression models included the following data: Current smoker (yes vs. no), alcohol intake (habitual drinker, nonhabitual drinker, or nondrinker), self-reported hepatitis-B virus (HBV) infection (yes/no), nephrotoxic drug use (yes/no), history of cardiovascular disease (yes/no), hypertension (yes/no), diabetes (yes/no), hyperuricemia (defined as uric acid >6.1 mg/dL), rural versus urban residency, body

mass index ≥25 kg/m^2 (yes/no) (calculated as measured weight in kilograms divided by the square of measured height in meters), plasma triglyceride level >1.7 mM (yes/no), plasma cholesterol level >5.2 mM (yes/no), plasma LDL-C level >3.64 mM (yes/no), and plasma HDL-C level <0.91 (yes/no).

Results

Characteristics of postmenopausal women

A total of 8573 postmenopausal women formed the study cohort. Compared to participants without indicators of kidney damage, subjects with CKD had the following characteristics: A more-advanced age; nephrotoxic medication use; a lower prevalence of self-reported HBV infection; a higher prevalence of cardiovascular disease, hypertension, and diabetes; elevated uric acid, triglyceride, creatinine, eGFR, ACR; a higher number of rural residents and a lower number of years in school [Table 1].

Prevalence of indicators of kidney function by disease stage

Among our cohort of 8573 postmenopausal women, the adjusted prevalence of an eGFR of <60 mL/min/1.73 m^2 was 5.3% (95% CI: 4.7–6.1) and that of albuminuria was 12.4% (95% CI: 11.7–13.1) [Table 2]. The overall adjusted prevalence of CKD among Chinese postmenopausal women in the cohort was 16.6% (95% CI: 15.8–17.4). In addition, the prevalence of kidney damage indicators at different CKD stages is presented in [Table 2]. The prevalence of an eGFR of 60–89 mL/min/1.73 m^2 was extremely high in cohort members with Stage 2 renal disease (47.7 [95% CI: 46.6–48.7]), and the prevalence of albuminuria was very high in cohort members with Stage 4 (42.9% [95% CI: 21.7–64.0]) and Stage 5 (45.5% [95% CI: 16.0–74.9]) renal disease.

Risk factors associated with indicators of kidney damage in postmenopausal women

We next analyzed factors associated with kidney damage indicators in our cohort of postmenopausal women. Logistic regression analysis revealed that the following factors were all associated with an eGFR lower than 60 mL/min/1.73 m^2 (the lower limit of multivariable adjusted ORs >1): Nephrotoxic drug use, a history of cardiovascular disease, and hyperuricemia [Table 3]. Hypertension and diabetes increased the chance of albuminuria being present (the lower limit of multivariable adjusted ORs >1; Table 3). In addition, the incidence of CKD was associated with nephrotoxic drug use, a history of cardiovascular disease, hypertension, diabetes, hyperuricemia, and triglyceride >1.7 mM (the lower limit of multivariable adjusted ORs >1; Table 3).

Table 1: Demographic and clinical characteristics of the postmenopausal cohort

	Participants with no indicators of kidney damage (*n*=7150) (%)	Participants with CKD (*n*=1423) (%)	*P*	Total (*n*=8573) (%)
Average age (years)	60.0±11.1	64.2±11.2	<0.001	60.7±11.2
Current smoker	392 (5.5)	89 (6.3)	0.26	481 (5.6)
Habitual drinker	156 (2.2)	22 (1.6)	0.20	178 (2.1)
Nonhabitual drinker	356 (5.0)	63 (4.4)		419 (4.9)
Self-reported HBV infection	161 (2.3)	28 (2.0)	0.009	189 (2.2)
Nephrotoxic medication use	298 (4.2)	88 (6.2)	0.001	386 (4.5)
History of cardiovascular disease	247 (3.5)	87 (6.1)	<0.001	334 (3.9)
Hypertension	3606 (50.5)	1000 (70.3)	<0.001	4606 (53.8)
Diabetes	739 (10.3)	253 (17.8)	<0.001	992 (11.6)
BMI (kg/m^2)	24.7 (3.8)	24.9 (4.1)	0.16	24.8 (3.8)
Uric acid (μM)	257.9 (70.8)	275.9 (92.3)	<0.001	261.5 (75.9)
Triglyceride (mM)	1.5 (1.2)	1.7 (1.6)	<0.001	1.5 (1.3)
LDL-C (mM)	3.1 (0.9)	3.1 (1.0)	0.81	3.1 (0.9)
HDL-C (mM)	1.4 (0.4)	1.4 (0.4)	0.02	1.4 (0.4)
Creatinine (μM)	69.0 (12.1)	84.5 (44.8)	<0.001	71.6 (22.1)
eGFR (ml/min/1.73 m^2)	94.9 (23.9)	81.8 (30.8)	<0.001	92.7 (25.7)
ACR (mg/g creatinine; median (IQR))	7.7 (3.0-14.1)	43.9 (30.5-85.9)	<0.001	9.1 (3.9-20.3)
Rural residents	3467 (48.5)	822 (57.8)	<0.001	4289 (50.0)
High school education or above	1840 (25.8)	199 (14.0)	<0.001	2039 (23.8)
Have health insurance	6562 (91.8)	1324 (93.0)	0.25	7886 (92.0)

Data are presented as number of cases (%) or mean±SD, unless stated otherwise. *P* values were analyzed for all parameters between participants with no indicators of kidney damage and participants with CKD. HBV=Hepatitis B virus; BMI=Body mass index; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; ACR=Albumin=creatinine ratio; IQR=Interquartile range; CKD=Chronic kidney disease; eGFR=Estimated glomerular filtration rate; SD=Standard deviation

Table 2: Prevalence of kidney function indicators in the postmenopausal cohort by disease stage

Disease stage	Kidney function			Albuminuria		CKD prevalence (95% CI)
	eGFR (ml/min/1.73 m²)	*n*	Prevalence (95% CI)	*n*	Prevalence (95% CI)	
1	>90	4027	47.0 (45.9-48.0)	512	12.7 (11.7-13.7)	6.0 (5.5-6.5)
2	60-89	4086	47.7 (46.6-48.7)	451	11.0 (10.1-12.0)	5.3 (4.8-5.7)
3	30-59	428	5.0 (4.5-5.5)	89	20.8 (17.0-24.6)	5.0 (4.5-5.5)
3a	45-59	377	4.4 (4.0-4.8)	73	19.4 (15.4-23.4)	4.4 (4.0-4.8)
3b	30-44	51	0.6 (0.4-0.8)	16	31.4 (18.6-44.1)	0.6 (0.4-0.8)
4	15-29	21	0.2 (0.1-0.4)	9	42.9 (21.7-64.0)	0.2 (0.1-0.3)
5	<15	11	0.1 (0.1-0.2)	5	45.5 (16.0-74.9)	0.1 (0.1-0.2)
Total		8573	100	1066	12.4 (11.7-13.1)	16.6 (15.8-17.4)

All prevalence data are adjusted for synthesized weights. eGFR=Estimated glomerular filtration rate; CKD=Chronic kidney disease; CI=Confidence interval

Table 3: Factors associated with indicators of kidney damage in the postmenopausal cohort

Factor	eGFR <60 ml/min/1.73 m²	Albuminuria	CKD	*P*
Current smoker	1.22 (0.84-1.78)	1.06 (0.79-1.44)	1.20 (0.94-1.55)	0.15
Habitual drinker	0.60 (0.27-1.32)	0.71 (0.42-1.19)	0.61 (0.38-0.98)	0.03
Nephrotoxic drug use	1.76 (1.20-2.56)	1.13 (0.84-1.52)	1.37 (1.06-1.76)	0.02
History of cardiovascular disease	1.66 (1.12-2.46)	1.19 (0.88-1.61)	1.33 (1.02-1.74)	0.03
Hypertension	1.15 (0.92-1.42)	2.59 (2.22-3.02)	2.07 (1.81-2.36)	<0.001
Diabetes	1.20 (0.90-1.59)	1.90 (1.58-2.27)	1.74 (1.47-2.05)	<0.001
Hyperuricemia	6.78 (5.21-8.83)	0.81 (0.62-1.06)	2.01 (1.64-2.47)	<0.001
Urban residents (vs. rural residents)	0.98 (0.78-1.22)	0.75 (0.65-0.86)	0.81 (0.71-0.92)	0.001
BMI (kg/m²) ≥25	0.71 (0.57-0.87)	1.10 (0.95-1.26)	0.98 (0.87-1.12)	0.78
Triglyceride (mM) >1.7	1.14 (0.92-1.43)	1.14 (0.98-1.33)	1.18 (1.03-1.35)	0.02
Cholesterol (mM) >5.2	1.19 (0.94-1.51)	0.91 (0.77-1.07)	0.98 (0.84-1.13)	0.73
HDL-C (mM) <0.91	0.70 (0.49-1.00)	0.96 (0.78-1.18)	0.89 (0.74-1.08)	0.25
LDL-C (mM) >3.64	1.02 (0.77-1.36)	1.10 (0.90-1.36)	1.07 (0.89-1.28)	0.47

Data are presented as multivariable-adjusted ORs (95% CI). Values with lower limits of multivariable adjusted ORs >1 are indicated in bold type. eGFR=Estimated glomerular filtration rate; BMI=body mass index; LDL-C=Low-density lipoprotein-cholesterol; HDL-C=High-density lipoprotein-cholesterol; CKD=Chronic kidney disease; BMI=Body mass index; CI=Confidence interval; ORs=Odds ratios

Discussion

This study surveyed 8573 postmenopausal women living in 13 provinces from different geographical regions of China. An analysis of CKD, lifestyle, and pathological factors associated with the disease in this cohort was conducted.

The association between postmenopausal women and CKD

The percentage of postmenopausal women among all initially recruited survey participants was approximately 18.2%. The overall adjusted prevalence of CKD was 16.6% (95% CI: 15.8–17.4) in this cohort of postmenopausal women, which is higher than the overall prevalence of CKD in Chinese adults (10.8% [95% CI: 10.2–11.3]) in 2012.[3] Moreover, it was found that the prevalence of an eGFR <60–89 mL/min/1.73 m² was extremely high in our cohort of postmenopausal women with Stage 2 renal disease, and that the prevalence of albuminuria was very high in our cohort of postmenopausal women with Stages 4 and 5 renal disease. These data indicate that the prevalence of kidney pathology is relatively high in postmenopausal women.

In addition, research indicates that menopause is associated with a high prevalence of osteoporosis, vertebral fractures, diabetes mellitus, and other diseases. Another association revealed by recent research is the occurrence of end-stage renal disease as an independent factor for earlier-onset menopause.[7] In mid-life women, moderate CKD has been linked to diminished cognitive performance.[8] Schopick *et al.* showed that long-term postmenopausal hormone use (>6 years) is associated with a reduced urinary ACR level in nondiabetic women, implying that postmenopausal hormone use may impact the renin-angiotensin system and renal endothelial function, therefore also influencing albumin excretion.[9]

Factors associated with indicators of kidney damage in postmenopausal women

Cardiovascular diseases are the most common causes of death in postmenopausal women with CKD.[10] Perticone *et al.* demonstrated in Southern-Italian postmenopausal women that impaired renal function, manifested by decreased eGFR, was associated with increased risks of cardiovascular events and mortality.[11] CKD has also been associated with cognitive impairment in menopausal women

with coronary artery disease; this impairment manifested in the areas of global cognition, executive function, language, and memory.[12] In perimenopausal women in their fifties, metabolic syndrome has also been associated with CKD.[2] In accordance with these observations, our study revealed that nephrotoxic drug use, history of cardiovascular disease, hyperuricemia, hypertension, and diabetes are all factors associated with CKD in Chinese postmenopausal women. Considering the use of nephrotoxic drug may worsen the renal function in CKD patients;[13] these drugs should be avoided or used with caution in postmenopausal women. It has been reported that the cardiovascular disease is the leading cause of mortality in women with Stage 5 CKD.[14] In addition, a recent study suggests that central obesity, in association with hypertension and diabetes, increases the risk of end-stage renal disease in postmenopausal women.[15] These findings support the view that cardiovascular diseases and impaired renal function may increase the risks of CKD in postmenopausal women. Nevertheless, the underlying mechanism still needs to be further elucidated.

Conclusion

Our research has demonstrated that the overall adjusted prevalence of CKD among our cohort of Chinese postmenopausal women was 16.6% (95% CI: 15.8–17.4), and it suggests that special attention should be focused onto postmenopausal women with nephrotoxic drug use, history of cardiovascular disease, hyperuricemia, hypertension, and diabetes. Hence, our findings may possibly provide valuable insights for disease prevention and management. However, because we did not measure the levels of gonadal hormones, such as estrogen, ongoing research will be conducted to more precisely explore this association between CKD prevalence and postmenopausal physiology and pathology.

Acknowledgments

This study was supported by the National Key Technology R and D Program of the Ministry of Science and Technology (Grant No. 2011BAI10B01), the National Key Technology R and D Program from the Ministry of Science and Technology (China; Grant No. 2007BAI04B10), Natural Science Foundation of Shandong Province (Grant No. ZR2012HQ001 and ZR2013HM100), and China Postdoctoral Science Foundation (Grant No. 21300073311146).

Financial support and sponsorship

Nil

Conflicts of interest

There are no conflicts of interest.

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