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Prevalence and Risk Factors for CKD: A Comparison Between the Adult Populations in China and the United States

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Introduction: Chronic kidney disease (CKD) is an important noncommunicable disease globally. Overall prevalence of CKD and distribution of its stages differ between countries. We postulate that these differences may not only be due to variation in prevalence of risk factors but also their differential impact in different populations or settings.

Methods: We used nationally representative data on the adult populations from both the United States (US; National Health and Nutrition Examination Survey [NHANES], 2009 to 2010, N = 5557) and China (China National Survey of CKD, 2009 to 2010, N = 46,949). Age, sex, central obesity, cardiovascular disease, diabetes, hypertension, and hyperuricemia were explored as candidate risk factors for CKD. The prevalence of CKD was calculated using survey weights.

Results: The prevalence of decreased estimated glomerular filtration rate (eGFR), defined as eGFR < 60 ml/min per 1.73 m^2, was 6.5% in the US versus 2.7% in China, whereas the prevalence of albuminuria (defined as urine albumin to creatinine ratio of $\geq$30 mg/g) was 8.1% in the US versus 9.5% in China. The distribution of eGFR categories differed between the countries ($P < 0.001$). Stronger associations of diabetes with both indicators were seen in the US participants, whereas stronger associations of male sex with both indicators and of hypertension with albuminuria were observed in the Chinese participants ($P <$ 0.05). After multivariable adjustment, a 65% change in prevalence difference for decreased eGFR was seen between China and the US.

Conclusion: People in China and the US share many common risk factors for CKD, but differences in prevalence and the potential impact of these risk factors for CKD were observed.

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CKD is recognized as a public health problem around the world. The burden of CKD has implications for the demand for renal replacement therapy and is associated with a higher risk of morbidity (especially due to cardiovascular disease), mortality, and hospitalization.[1,2] Prevalence estimates for CKD based on population-based screening programs have been published by a number of countries and regions, including developed countries such as the United States (US), Australia, Canada, Norway, Japan, and South Korea, as well as the developing countries such as China and Latin America.[3–10] Overall, the prevalence of CKD is seen to vary from 8% to 16%.[2] Possible explanations for this variation include differences in ethnicities,[11,12] socioeconomic status,[13,14] risk factors,[6,15] and genetic susceptibility to renal damage.[16,17] Moreover, definitions of CKD have varied among these studies, and have likely influenced the true differences in the prevalence of CKD across nations.

In this study, we sought to compare the prevalence of CKD between China and the US, using nationally representative datasets from each country. We postulated that differences in the prevalence of CKD between these 2 countries would not only be related to differences in the prevalence of risk factors for CKD, but

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could also be due to variations in the strength of the associations with risk factors within each country. The goals of our study were to compare the prevalence of CKD, the prevalence of risk factors for CKD, and the magnitude of the associations between the risk factors for and prevalence of CKD between these 2 countries.

METHODS

Study Population

This study used cross-sectional data from 2 nationally representative data sources. Data for China were taken from the China National Survey of CKD, which has been described in detail previously.[8] In this study, a national representative sample of adults was drawn using a multistage, stratified sampling method. First, 13 provinces from different geographical regions in China were selected. Then 1 urban and 1 rural district were drawn in each province, and 3 subdistricts were randomly selected from each district. Five communities were randomly selected from each subdistrict. Finally, individuals were randomly chosen from each community. Altogether, 50,550 people were invited. All on-site screening and laboratory testing was performed between 2009 and 2010. Data for the US were taken from the NHANES, a cross-sectional survey of the health and nutritional status of the civilian, noninstitutionalized population of the US. Participants are randomly selected through a complex, multistage, cluster-sampling probability design. First, 1 county was selected from each of 15 county groups (based on their characteristics) in the US. Twenty to 24 smaller groups (with a large number of households in each group) were then selected from each county. Within each group, 30 households are selected. A computer algorithm randomly selects some, all, or none of the household members to participate in the survey. The survey examines a nationally representative sample of about 5000 persons over the age of 20 years in each cohort. Our study analyzed data from NHANES 2009 to 2010.[18]

In both surveys, participants completed questionnaires and underwent a medical evaluation. Participants who had missing data on serum creatinine or albuminuria, were less than 20 years of age, or reported being pregnant at the time of the study, were excluded from the analysis, leaving a sample of 46,949 individuals from China and 5557 individuals from the US. The ethics committee of Peking University Health Science Center and the institutional review board of University of Michigan approved the study.

Study Variables

Assessment of Kidney Damage

We used the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to calculate the eGFR.[19] Decreased eGFR was defined as eGFR $<$ 60 ml/min per 1.73 m^2. Serum creatinine in both NHANES and the China National Survey of CKD was measured using a kinetic rate Jaffe method. The creatinine calibration for NHANES 2009 to 2010 is traceable to an isotope dilution mass spectrometry reference method.[20] Serum creatinine measurements in the Chinese study were processed in a central laboratory in each enrolled province. Samples were calibrated at the laboratory of Peking University First Hospital (Beijing, China), where the creatinine calibration used is traceable to the isotope dilution mass spectrometry reference method. As a sensitivity analysis, we also examined eGFR calculated by an equation developed for Chinese CKD patients based on an adaptation of the Modification of Diet in Renal Disease equation.[21]

Albuminuria was defined by a urine albumin to creatinine ratio (UACR) of 30 mg/g or higher. Microalbuminuria was defined as an UACR of 30 mg/g to 299 mg/g, and macroalbuminuria was defined as an UACR of 300 mg/g or higher. In China, urinary albumin was measured with immunoturbidimetric tests from a morning spot urine sample. Urinary creatinine was measured by a kinetic rate Jaffe method. For NHANES 2009 to 2010, a solid-phase fluorescent immunoassay was used for the measurement of urinary albumin from a random spot urine sample.[22] Urinary creatinine was measured using the Roche/Hitachi Modular P chemistry analyzer (Roche Diagnostics, Indianapolis, IN). We did not use data from first-morning void UACR in NHANES 2009 to 2010, because of a high percentage (15%) of missing data.

CKD was defined by the presence of either decreased eGFR or albuminuria. Staging of CKD was done following the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of CKD.[23]

Assessment of Possible Risk Factors

Blood pressure was measured by trained physicians or assistants using standard methods (mercury sphygmomanometry and appropriately sized arm cuffs) after 5 minutes of sitting. Multiple measurements were taken at 5-minute intervals. The mean of the 3 measurements of blood pressure was calculated unless the differences among the readings were greater than 10 mm Hg. In that case, the mean of the 2 closest readings was used. Individuals were considered hypertensive if they had a systolic blood pressure of 140 mm Hg or more, if they had a diastolic blood pressure of 90 mm Hg or more, if they reported taking antihypertensive medication at the time of interview, or if they had a self-reported history of hypertension. Diabetes mellitus was defined as fasting plasma glucose of 7.0 mmol/l (126 mg/dl) or more, any use of insulin or oral hypoglycemic medication despite fasting plasma glucose level, or any self-reported history of diabetes. Height and weight were used to calculate body mass index (BMI; weight/height^2 [kg/m^2]). Obesity was defined as BMI greater than 25 kg/m^2 for Chinese participants[24] and 30 kg/m^2 for NHANES participants.[25] We defined central obesity based on the measurement of waist circumference. Waist circumference greater than 80 cm for women or 90 cm for men in Chinese population,[26] or 88 cm for women or 102 cm for men in the US population,[25] were considered to have central obesity. We used separate cut-off values for the 2 countries in defining obesity and central obesity to reflect ethnic diversity in body composition. Cardiovascular disease (CVD) was defined by the self-reported events of previous myocardial infarction or stroke according to questionnaire responses for the question "Have you ever been diagnosed to have myocardial infarction or stroke?" The definition of a current smoker was based on the answer to the question "Do you now smoke cigarettes?" Hyperuricemia was defined by plasma uric acid concentration greater than 422 μmol/l (7.09 mg/dl) for men and greater than 363 μmol/l (6.10 mg/dl) for women.[27]

Statistical Analysis

The analysis was performed with appropriate sampling weights in each country to obtain unbiased prevalence estimates from complex survey design in each country. In accordance with the NHANES analytic guidelines, sample weights, strata, and primary sampling unit variables were used to account for unequal probabilities of selection and the multistage, stratified sample design.[28] A synthesized weight for China was calculated based on sampling weight, a nonresponse weight, and a population weight. The weighted prevalence of low eGFR, albuminuria, and total CKD in different stages are reported.

Weighted logistic regression models were used separately in each country to investigate the associations between the potential risk factors and each CKD indicator, that is, decreased eGFR or albuminuria. Multivariable adjusted odds ratios (ORs) were reported with 95% confidence intervals (CIs). The candidate variables included age, sex, black race (in the US model only), current smoking, cardiovascular disease, CVD, hypertension, diabetes mellitus, hyperuricemia, and central obesity.

A combined sample dataset from both countries was created, and multivariable modified Poisson regression was used to estimate adjusted associations (prevalence ratios [PRs]) for each risk factor of CKD.[29] Interaction terms between country and each risk factor were examined in these models to evaluate differences in effect size by country. Risk factors in the model included all risk factors listed above, except smoking, as it was not statistically significant for any of the indicators of CKD in the combined dataset or that stratified by country. A weighted logistic regression model was used to explore the change in PR between countries before and after adjustment for risk factors. The prevalence difference for indicators of CKD attributed by the risk factors between the 2 countries was expressed as (unadjusted PR−adjusted PR)/(unadjusted PR−1).[30]

Sensitivity analyses were performed with the eGFR calculated by the modified Modification of Diet in Renal Disease equation for the Chinese participants and simplified Modification of Diet in Renal Disease equation for the NHANES participants.[31] All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). In hypothesis testing, P values are 2-sided, and a P value of less than 0.05 was considered significant.

RESULTS

Demographic Characteristics

Table 1 displays the weighted mean demographic variables by country. Mean age in the Chinese population was younger than that of the US (42.6 years vs. 47.2 years, $P < 0.001$). The sex distribution was similar in the 2 national samples. The Chinese population was shorter and slimmer compared with the US population. The prevalence of hypertension, diabetes, CVD, hyperuricemia, and obesity were all higher in the US population than those in China.

Prevalence of CKD and Distribution of Stages Between Countries

Differences were observed in the prevalence of CKD between countries. The adjusted prevalence of decreased eGFR (<60 ml/min per 1.73 m^2) in the US was 6.5% (95% CI = 5.5%−7.5%), which was 1.5 times higher than that in China (2.7%, 95% CI = 2.5%−2.9%, $P < 0.001$). In contrast, China had an adjusted prevalence of albuminuria of 9.5% (95% CI = 8.9%−10.0%), which was higher than that in the US (8.1%, 95% CI = 6.8%−9.4%, $P = 0.004$). The overall prevalence of CKD was 11.6% in China and 12.9% in the US, respectively ($P = 0.047$) (Figure 1). Table 2 shows a cross-tabulation of eGFR and albuminuria categories according to the Kidney Disease: Improving Global Outcomes prognostic classification of CKD.

Association of Risk Factors With Each Indicator of CKD Between Countries

The results of the multivariable logistic regression model stratified by country showing the differential association of risk factors with each indicator of CKD are displayed in Table 3. Older age, self-reported

Table 1. Comparison of demographic characteristics in China and United States (US)

	China		US		
Characteristic	N	Mean (SE) or %	n	Mean (SE) or %	*P* value
Age, yr	46949	42.6 (0.15)	5557	47.2 (0.51)	<0.001
Male, %	46949	50.0	5557	49.0	0.06
Black, %	—	—	5557	10.6	
Education to high school or above	46832	31.4	5546	81.2	<0.001
Health insurance, %	45371	93.5	5552	79.1	<0.001
Height, cm	46661	161.9 (0.08)	5519	168.9 (0.21)	<0.001
Weight, kg	46648	61.8 (0.10)	5522	82.2 (0.42)	<0.001
BMI, kg/m^2	46637	23.5 (0.03)	5514	28.7 (0.13)	<0.001
Waist, cm	46148	80.6 (0.09)	5337	98.2 (0.44)	<0.001
Current smoker, %	46949	24.9	5557	20.3	<0.001
Obesity, %	16617	16.6	5514	35.7	<0.001
Central obesity, %	46148	34.1	5337	53.9	<0.001
Diabetes, %	46904	5.0	5557	10.7	<0.001
Hypertension, %	46708	30.4	5557	35.1	<0.001
Systolic BP, mm Hg	46679	125.2 (0.18)	5296	120.3 (0.51)	<0.001
Diastolic BP, mm Hg	46677	80.1 (0.10)	5296	69.2 (0.71)	<0.001
CVD, %	42087	2.0	5557	5.2	<0.001
Triglyceride, mg/dl	46909	128.87 (1.13)	2690	127.23 (2.41)	0.60
LDL cholesterol, mg/dl	41475	99.74 (0.35)	2642	116.02 (0.95)	<0.001
HDL cholesterol, mg/dl	41536	53.65 (0.17)	5557	53.05 (0.44)	0.12
Uric acid, mg/dl	33032	4.62 (0.01)	5557	5.47 (0.03)	<0.001
Hyperuricemia, %	33032	7.9	5557	18.5	<0.001
Creatinine, mg/dl	46949	0.85 (0.002)	5557	0.88 (0.006)	<0.001
eGFR, ml/min per 1.73 m^2	46949	97.3 (0.19)	5557	94.1 (0.69)	<0.001
ACR, mg/g; median [IQR])	46949	6.7 (1.91–18.62)	5557	5.97 (3.91–10.53)	<0.001

ACR, urine albumin:creatinine ratio; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein.

history of CVD, diabetes, and hyperuricemia were all independently associated with eGFR < 60 ml/min per 1.73 m^2 in both countries, whereas being female was associated with decreased eGFR in China but not in the US. Hypertension was a significant risk factor for decreased eGFR for the US population but not in the Chinese population. For albuminuria, both the US and China shared the common risk factors of age, hypertension, and diabetes. Although female sex and central obesity were independently associated with albuminuria among the Chinese, they were not significantly associated with albuminuria in the US population.

In Table 4, we compared PRs and the interaction of each of the risk factors for CKD between countries in the combined dataset from both Chinese and NHANES participants. Age, diabetes, CVD, and hyperuricemia were common risk factors for decreased eGFR, whereas age, hypertension, and diabetes were common risk factors for albuminuria in both countries. Significant interactions of age, sex, and diabetes for decreased eGFR were found between countries (all *P* values for interaction <0.05). Age and diabetes showed a larger association with decreased eGFR in the US than in China, whereas male sex showed a higher protective association with decreased eGFR in China than in the US. Regarding albuminuria, significant interactions were found between countries for sex, hypertension, and diabetes (all *P* values for interaction <0.05). There was a greater association of hypertension with albuminuria in China than in the US, whereas diabetes showed a greater association in the US than in China.

Prevalence Difference Between Countries

We assessed the difference in prevalence between the US and China attributable to CKD risk factors. After adjusting for age and sex, the PR (China vs. US) for decreased eGFR rose from 0.40 (95% CI = 0.35−0.46)

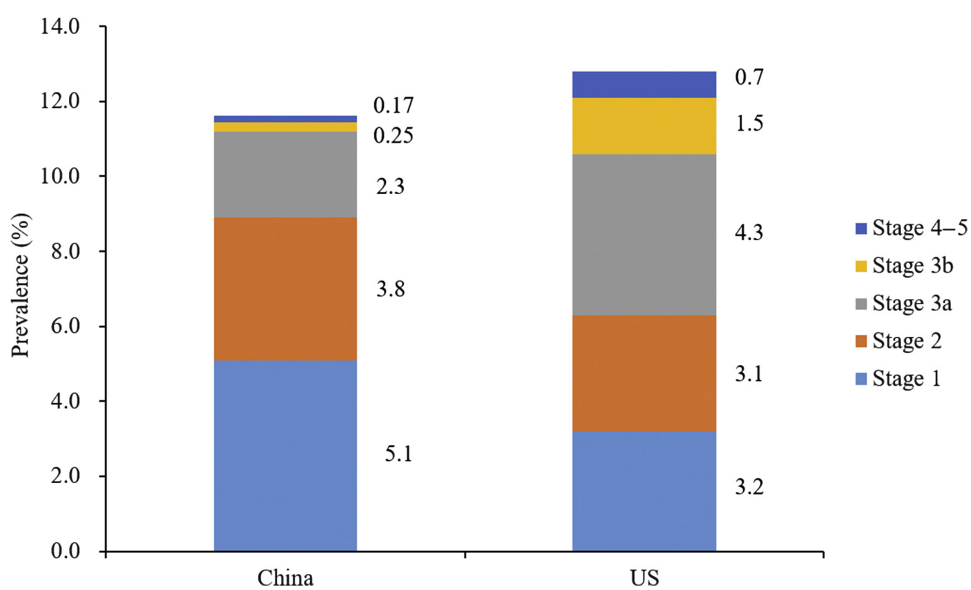

Figure 1. Weighted prevalence of chronic kidney disease between China and the United States (US).

Table 2. Weighted prevalence of chronic kidney disease in China and the United States

eGFR category (ml/min per 1.73 m^2)	Albuminuria category A1 (<30 mg/g)	A2 (30–299 mg/g)	A3 (≥300 mg/g)	Total
China				
≥90	57.6% (56.7%–58.4%)	4.9% (4.5%–5.3%)	0.3% (0.2%–0.3%)	62.7% (61.8%–63.6%)
60–89	30.8% (30.0%–31.6%)	3.5% (3.1%–3.8%)	0.3% (0.2%–0.4%)	34.6% (33.8%–35.4%)
45–59	1.8% (1.7%–2.0%)	0.4% (0.29%–0.48%)	0.05% (0.02%–0.08%)	2.3% (2.1%–2.5%)
30–44	0.17% (0.11%–0.22%)	0.07% (0.03%–0.11%)	0.01% (0.003%–0.02%)	0.25% (0.18%–0.32%)
15–29	0.10% (0.03%–0.14%)	0.03% (0.001%–0.05%)	0.02% (0.001%–0.04%)	0.14% (0.07%–0.21%)
<15	0.02% (0.001%–0.03%)	0.005% (0.001%–0.01%)	0.01% (0.001%–0.03%)	0.03% (0.01%–0.06%)
Total	90.00% (89.44%–90.55%)	9.30% (8.76%–9.85%)	0.70% (0.56%–0.85%)	100%
United States				
≥90	57.3% (55.7%–58.9%)	3.0% (2.5%–3.5%)	0.2% (0.1%–0.4%)	60.6% (59.0%–62.2%)
60–89	29.8% (28.2%–31.3%)	2.6% (2.1%–3.1%)	0.5% (0.3%–0.8%)	32.9% (31.4%–34.5%)
45–59	3.6% (3.0%–4.1%)	0.7% (0.5%–0.9%)	0.1% (0.03%–0.18%)	4.3% (3.8%–4.9%)
30–44	0.9% (0.7%–1.2%)	0.5% (0.3%–0.6%)	0.06% (0.01%–0.11%)	1.5% (1.2%–1.8%)
15–29	0.3% (0.1%–0.4%)	0.2% (0.1%–0.3%)	0.1% (0.02%–0.19%)	0.5% (0.4%–0.7%)
<15	0.02% (0.000%–0.05%)	0.05% (0.000%–0.1%)	0.08% (0.06%–0.2%)	0.2% (0.06%–0.24%)
Total	91.9% (91.1%–92.7%)	7.0% (6.2%–7.7%)	1.1% (0.8%–1.4%)	100%

Data are prevalence and 95% confidence interval. eGFR, estimated glomerular filtration rate.

to 0.57 (95% CI = 0.48−0.67) (Table 5). After further adjustment for hypertension, diabetes, CVD, central obesity and hyperuricemia, PR increased to 0.79 (95% CI = 0.58−0.90), which represents a 65% change in prevalence difference between China and the US, indicating that approximately two-thirds of the difference in prevalence can be explained by differences in the distributions of risk factors. After adjustment for all these covariates, PR (China vs. US) for albuminuria changed from 1.12 (95% CI = 1.06−1.35) to 1.35 (95% CI = 1.15−1.59), suggesting that differences in risk factors may not explain the difference in prevalence of albuminuria observed. In the sensitivity analysis with the eGFR calculated by the Modification of Diet in Renal Disease equation, interaction of risk factors for decreased eGFR between countries were also seen (see Supplementary Table S2). After adjustment for all of these covariates, PR changed from 0.30 (95% CI = 0.25−0.36) to 0.59 (95% CI =0.43−0.74), which represented a 41% change in prevalence difference between China and the US.

DISCUSSION

This international study represents a comparative epidemiologic analysis between 2 large, contemporaneous, nationally representative samples from China and the US, specifically with a view to (i) examining the prevalence of CKD and its risk factors between the 2 countries, and (ii) assessing the relative strength of associations of the established risk factors for CKD between the 2 countries. Consistent with our hypothesis, we observed a lower adjusted prevalence of decreased eGFR in China compared to the US. On the other hand, there was a higher adjusted prevalence of albuminuria in China compared to the US. Importantly, nearly two-thirds (65%) of the difference in adjusted prevalence of decreased eGFR between the countries

Table 3. Weighted odds ratios for decreased estimated glomerular filtration rate (eGFR) and albuminuria by risk factors stratified by country

	Decreased eGFR						Albuminuria					
	China			United States			China			United States		
Risk factor	OR	95% CI	*P* value	OR	95% CI	*P* value	OR	95% CI	*P* value	OR	95% CI	*P* value
Age, per 10 yr	2.20	2.02–2.39	<0.001	3.92	3.41–4.51	<0.001	1.12	1.06–1.18	<0.001	1.20	1.11–1.30	<0.001
Male	0.43	0.32–0.57	<0.001	0.70	0.45–1.06	0.09	0.82	0.68–0.98	0.03	1.10	0.70–1.72	0.68
Black	—	—	—	1.22	0.87–1.71	0.24	—	—	—	1.34	0.89–1.81	0.06
Smoking	0.75	0.54–1.04	0.09	1.05	0.60–1.84	0.87	1.19	0.87–1.45	0.09	1.32	0.93–1.87	0.12
Hypertension	1.04	0.77–1.24	0.16	1.48	1.09–2.37	0.03	2.48	2.12–2.89	<0.001	1.99	1.48–2.67	<0.001
Diabetes	1.43	1.09–2.05	0.02	1.68	1.20–2.37	<0.003	2.00	1.64–2.46	<0.001	2.56	2.01–3.25	<0.001
CVD	2.21	1.37–3.59	0.001	2.05	1.32–3.20	0.002	1.09	0.75–1.59	0.66	1.32	0.92–1.90	0.24
Hyperuricemia	7.22	5.50–9.47	<0.001	4.70	3.13–6.59	<0.001	0.93	0.74–1.17	0.52	1.05	0.81–1.36	0.71
Central obesity	1.08	0.85–1.37	0.52	0.81	0.61–1.07	0.12	1.20	1.03–1.40	0.02	0.94	0.73–1.19	0.58

CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio.

Table 4. Comparison of prevalence ratios by country by risk factors in the combined dataset for decreased estimated glomerular filtration rate (eGFR) and albuminuria

Risk Factor	China		United States		*P* value for interaction
	PR	95% CI	PR	95% CI	
Decreased eGFR					
Age, per 10 yr	2.07	1.98–2.16	2.61	2.38–2.87	<0.001
Male	0.60	0.53–0.68	0.85	0.69–1.05	0.005
Hypertension	1.15	0.97–1.32	1.52	1.21–2.91	0.13
Diabetes	1.13	1.03–1.28	1.48	1.29–1.61	0.03
CVD	1.36	1.12–1.65	1.39	1.18–1.64	0.87
Hyperuricemia	2.73	2.44–3.04	2.49	2.13–2.91	0.35
Central obesity	1.09	0.98–1.22	0.94	0.79–1.11	0.15
Albuminuria					
Age, per 10 yr	1.15	1.12–1.18	1.15	1.08–1.22	0.94
Male	0.83	0.73–0.92	1.37	0.93–1.66	<0.001
Hypertension	2.55	2.34–2.81	1.80	1.54–2.24	0.02
Diabetes	1.73	1.56–1.92	2.32	1.96–2.76	0.01
CVD	0.94	0.81–1.13	1.06	0.85–1.21	0.51
Hyperuricemia	0.89	0.73–1.15	1.21	0.97–1.44	0.22
Central obesity	1.28	1.18–1.39	1.03	0.86–1.28	0.23

CI, confidence interval; CVD, cardiovascular disease; PR, prevalence ratio.

was accounted for by the prevalence and magnitude of the association of CKD with its risk factors, including age, sex, diabetes, hypertension, central obesity, CVD, and hyperuricemia.

One of the major differences in the prevalence of CKD between China and the US was the much lower prevalence of decreased eGFR in China. CKD was predominantly in the early stages (stages 1–2) in China, which was also observed in surveys in Italy and Norway.[6,32] In the US, the prevalence of moderate to advanced CKD (stages 3–5) was remarkably higher. Compared with the US sample (mean age 47.2 years) and the Norwegian sample (mean age 50.2 years),[6] the Chinese sample was considerably younger (mean age 42.6 years). We observed a greater association between age and decreased eGFR in the US compared to China. However, the age and sex differences between the countries could explain only a smaller proportion (28%) of the difference in CKD prevalence. The higher prevalence of risk factors including diabetes, hypertension, central obesity, CVD, and hyperuricemia contributed to the higher prevalence of decreased renal function in the US.

We noticed differences in association between 2 of the major risk factors—namely, hypertension and diabetes—and CKD indicators, eGFR, and albuminuria. Diabetes was much more strongly associated with both decreased eGFR and albuminuria in the US than in China. This could potentially be the result of the different durations of diabetes (5.2 years for China vs. 11.7 years for the US). Hypertension was more strongly associated with albuminuria in China than in the US. We believe that, barring the potential influence of genetic factors and/or the higher prevalence of glomerulonephritis, poor control of hypertension could likely be closely related to the greater prevalence of albuminuria in the Chinese population. Recent analyses have illustrated the rates of awareness, treatment, and control of hypertension in China were 42.6%, 34.2%, and 9.3%, respectively,[33] which were all much lower than those in NHANES 2003 to 2004 in the US, with the corresponding rates of 66.5%, 53.7%, and 33.1%, respectively.[34] In our analysis, there was no significant interaction of hypertension as a risk factor for decreased eGFR between countries, but the potential influence of hypertension on renal function in China cannot be ignored. The average durations of hypertension were 5.8 years for China and 11.7 years for the US in our study. In a previous study, hypertension was associated with decreased eGFR if the history of hypertension exceeded 10 years in the Chinese population.[35]

Central obesity is another major risk factor for noncommunicable diseases, and was found in our study to be independently associated with albuminuria in the Chinese sample. Obesity may promote kidney damage by increasing the risk of diabetes and hypertension or by means of an independent pathway. Obesity can also directly induce glomerular hyperperfusion and hyperfiltration, with resultant increased urinary albumin excretion.[36,37] Chinese and Caucasians have different body fat distribution, which may not be reflected by BMI. The Chinese have been observed to have a greater volume of subcutaneous abdominal adipose tissue and visceral adipose tissue than individuals of white race/ethnicity, even at the same BMI level.[38] As a more sensitive parameter to reflect adiposity, we used waist circumference instead of BMI in the current study. Adiposity is rapidly becoming an important public health problem in China. The prevalence of abdominal obesity increased from 8.5% to 27.8% among men and from 27.8% to 45.9% among women

Table 5. Changes of prevalence ratio of chronic kidney disease after adjustment for risk factors (China versus the United States)

Model	PR (95% CI)	*P* value
Decreased eGFR		
Unadjusted	0.40 (0.35–0.46)	<0.001
Adjusted for age and sex	0.57 (0.48–0.67)	<0.001
Adjusted for multivariables[a]	0.79 (0.58–0.90)	0.005
Albuminuria		
Unadjusted	1.12 (1.06–1.35)	0.004
Adjusted for age and sex	1.44 (1.26–1.64)	<0.001
Adjusted for multivariables[a]	1.35 (1.15–1.59)	0.003

CI, confidence interval; eGFR, estimated glomerular filtration rate; PR, prevalence ratio.
[a]Variables in the model were age, sex, hypertension, diabetes, central obesity, hyperuricemia, and cardiovascular disease.

during the period of 1993 to 2009.[39] Although data from NHANES 1998 to 2008 showed an upward trend of obesity among US males, no significant trend has been observed among females.[40] This has obvious implications for the future burden of chronic diseases such as CKD in China.

The risk factors examined in this study (diabetes, hypertension, CVD, hyperuricemia, obesity) were shown to explain some of the difference in prevalence of decreased eGFR between the counties. These variables, together with age and sex, explained 65% of the difference in prevalence. This information has public health implications for both countries. For the US, it provides confidence that carrying out campaigns to prevent common chronic disorders could potentially lower the burden of decreased renal function. For China, owing to its changing demographic profile, it is a warning of a future rise in the prevalence of loss of renal function. With higher life expectancies, the Chinese population is currently in the process of aging. It has been estimated that by 2030, 16% of the Chinese citizens will be 65 years or more of age, whereas in 2000, this figure was only 7%.[41] Along with aging and lifestyle changes, rapid increases in the prevalence of noncommunicable diseases such as hypertension and diabetes have been observed. In the 1990s, the prevalences of hypertension and diabetes were only 11% and 2.5%, respectively,[42,43] whereas the rates have now reached 30% and 11.6%, respectively, in recent surveys.[33,44] A greater burden of renal functional impairment will not only increase the burden of end-stage kidney disease, but will also increase the risk of premature death and/or cardiovascular events.[2] The so called "disease-multiplier" effect will additionally consume disproportionate health care budgets and public resources in controlling CKD.

The candidate risk factors in our studies did not explain much of the prevalence difference of albuminuria between China and the US. There are other risk factors that were not captured by our study, which could potentially be responsible for this difference. Previous studies indicated that the reference range for ACR is subject to racial differences.[45,46] It has been found that the kidney risk variant of *APOL1* accounted for a large part of the disparity in the progression of nondiabetic kidney disease among Africans but not among Asians.[47] The interaction analysis model that we explored did not take race into account, as the racial composition of China and the US are quite different and are not strictly comparable. Some social—environment factors have been reported to be associated with CKD. Dietary patterns with higher intake of red meats, saturated fats, and sweets were previously reported to be associated with microalbuminuria.[48] There is also evidence for an association between environmental second-hand smoking exposure and/or environmental heavy metal exposure and/or particulate matter air pollution and CKD.[49–51]

Our study has some limitations. First, the indicators of CKD were based on single measurements. Fresh morning urine samples were available in the Chinese cohort, whereas random urine samples were collected in the US NHANES sample. Given the biological variation and other pathological and physiological causes of albuminuria, (e.g., stress, inflammation),[52] repeated measurements of ACR are recommended to avoid overestimation of the prevalence of albuminuria. Furthermore, differences have been observed for variability between void morning urine sample—based and random urine sample—based estimates of albuminuria. It is believed that the first morning sample may correlate better with the 24-hour urine than the random sample, but both methods have been recommended by Kidney Disease: Improving Global Outcomes.[53] In addition, the methods for the measurement of urinary albumin and creatinine and the calibration method were not consistent between China and the US. For the measurement of creatinine, the NHANES value was calibrated traceable to an isotope dilution mass spectrometry reference method. In China, the calibration was indirect, with all the central laboratories in each province calibrating their measurements of creatinine to Peking University First Hospital, whereas the US measurements were calibrated to the Cleveland Clinic Laboratory value. The discordant methodology may introduce some bias into the results, but this should be minimized by the fact that UACR was analyzed as a categorical variable. Second, the definition of diabetes was based on self-reported history and fasting plasma glucose level. Oral glucose tolerance test results or plasma HbA_1C levels were not available to confirm the diagnosis of diabetes in the Chinese population. For the NHANES study, fasting plasma glucose levels were missing in among approximately one-half of the sample population. Therefore, the prevalence of diabetes and its association with CKD is likely to have been underestimated. Finally, the cross-sectional design of the study makes it impossible to assign causality between indicators of CKD and associated risk factors.

To the best of our knowledge, this is the first study to directly compare the burden of CKD and its risk factors between China and the US. The large sample sizes and the representative sampling methodologies of the 2 surveys added statistical power to the study. There is a higher prevalence of early stages of CKD and a lower prevalence of decreased renal function in China compared to the US. This suggests there may still be an opportunity for China to use interventional strategies to reduce the future burden of CKD. China and the US share many common risk factors of CKD, but with differential prevalences and impact potentials for the development of CKD. The precise reasons for these observations will need to be investigated further. It behooves public health authorities in both countries to integrate CKD prevention programs into their national public health surveillance and health promotion and disease prevention programs, to control the public health burden of noncommunicable diseases as a whole and CKD in particular.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Table S1. Weighted odds ratios for decreased estimated glomerular filtration rate (eGFR) by risk factors, stratified by country.

Table S2. Comparison of prevalence ratios by country by risk factors in the combined dataset for decreased estimated glomerular filtration rate (eGFR).

Table S3. Changes in prevalence ratio of decreased estimated glomerular filtration rate (eGFR) after adjustment for risk factors (China vs. US).

Supplementary material is linked to the online version of the paper at www.kireports.org.

REFERENCES

1. Ayodele OE, Alebiosu CO. Burden of chronic kidney disease: an international perspective. *Adv Chronic Kidney Dis*. 2010;17:215–224.
2. Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. *Lancet*. 2013;382:260–272.
3. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA*. 2007;298:2038–2047.
4. White SL, Polkinghorne KR, Atkins RC, et al. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD Epidemiology Collaboration (CKD-EPI) and Modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (Australian Diabetes, Obesity and Lifestyle) Study. *Am J Kidney Dis*. 2010;55:660–670.
5. Arora P, Vasa P, Brenner D, et al. Prevalence estimates of chronic kidney disease in Canada: results of a nationally representative survey. *CMAJ*. 2013;185:E417–E423.
6. Hallan SI, Coresh J, Astor BC, et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. *J Am Soc Nephrol*. 2006;17:2275–2284.
7. Imai E, Horio M, Watanabe T, et al. Prevalence of chronic kidney disease in the Japanese general population. *Clin Exp Nephrol*. 2009;13:621–630.
8. Zhang L, Wang F, Wang L, et al. Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet*. 2012;379:815–822.
9. Gutierrez-Padilla JA, Mendoza-Garcia M, Plascencia-Perez S, et al. Screening for CKD and cardiovascular disease risk factors using mobile clinics in Jalisco, Mexico. *Am J Kidney Dis*. 2010;55:474–484.
10. Lee SW, Kim YC, Oh SW, et al. Trends in the prevalence of chronic kidney disease, other chronic diseases and health-related behaviors in an adult Korean population: data from the Korean National Health and Nutrition Examination Survey (KNHANES). *Nephrol Dial Transplant*. 2011;26:3975–3980.
11. Freedman BI. End-stage renal failure in African Americans: insights in kidney disease susceptibility. *Nephrol Dial Transplant*. 2002;17:198–200.
12. Tarver-Carr ME, Powe NR, Eberhardt MS, et al. Excess risk of chronic kidney disease among African-American versus white subjects in the United States: a population-based study of potential explanatory factors. *J Am Soc Nephrol*. 2002;13:2363–2370.
13. Gonzalez Villalpando C, Stern MP, Arredondo Perez B, et al. Nephropathy in low income diabetics: the Mexico City Diabetes Study. *Arch Med Res*. 1996;27:367–372.
14. Vart P, Gansevoort RT, Coresh J, et al. Socioeconomic measures and CKD in the United States and The Netherlands. *Clin J Am Soc Nephrol*. 2013;8:1685–1693.
15. Correa-Rotter R, Wesseling C, Johnson RJ. CKD of unknown origin in Central America: the case for a Mesoamerican nephropathy. *Am J Kidney Dis*. 2014;63:506–520.
16. Smith SR, Svetkey LP, Dennis VW. Racial differences in the incidence and progression of renal diseases. *Kidney Int*. 1991;40:815–822.
17. Freedman BI, Espeland MA, Heise ER, et al. Racial differences in HLA antigen frequency and hypertensive renal failure. *Am J Hypertens*. 1991;4:393–398.
18. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2015. Available at: https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/Default.aspx?BeginYear=2009. Accessed July 15, 2015.
19. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150:604–612.
20. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2015. Available at: http://www.cdc.gov/NCHS/data/nhanes/nhanes_09_10/BIOPRO_F_met_creatinine.pdf. Accessed July 15, 2015.

21. Ma YC, Zuo L, Chen JH, et al. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *J Am Soc Nephrol*. 2006;17:2937–2944.

22. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2015. Available at: http://www.cdc.gov/nchs/data/nhanes/nhanes_09_10/lab.pdf. Accessed July 15, 2015.

23. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3:1–150.

24. World Health Organization Western Pacific Region, International Association for the Study of Obesity/International Obesity Task Force. The Asia-Pacific Perspective: Redefining Obesity and Its Treatment. Melbourne: Health Communications Australia; 2000.

25. WHO/FAO. Report of the Joint WHO/FAO Expert Consultation. Expert Consultation on Diet, Nutrition and the Prevention of Chonic Disease. Geneva: World Health Organization; 2003.

26. Alberti KG, Zimmet P, Shaw J, et al. The metabolic syndrome–a new worldwide definition. *Lancet*. 2005;366:1059–1062.

27. Li Q, Li X, Kwong JS-W, et al. Diagnosis and treatment for hyperuricaemia and gout: a protocol for a systematic review of clinical practice guidelines and consensus statements. *BMJ Open*. 2017;7:e014928.

28. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Data. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2015. Available at: http://www.cdc.gov/nchs/tutorials/nhanes/SurveyDesign/Weighting/intro.htm. Accessed July 15, 2015.

29. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159:702–706.

30. Morgenstern H. Attributable fractions. In: Boslaugh S, ed. *Encyclopedia of Epidemiology*. vol. 1. Thousand Oaks, CA: Sage Publications; 2008:55–63.

31. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130:461–470.

32. De Nicola L, Donfrancesco C, Minutolo R, et al. Prevalence and cardiovascular risk profile of chronic kidney disease in Italy: results of the 2008-12 National Health Examination Survey. *Nephrol Dial Transplant*. 2015;30:806–814.

33. Wang J, Zhang L, Wang F, et al. Prevalence, awareness, treatment, and control of hypertension in China: results from a national survey. *Am J Hypertens*. 2014;27:1355–1361.

34. Ong KL, Cheung BM, Man YB, et al. Prevalence, awareness, treatment, and control of hypertension among United States adults 1999-2004. *Hypertension*. 2007;49:69–75.

35. Zhang L, Zhang P, Wang F, et al. Prevalence and factors associated with CKD: a population study from Beijing. *Am J Kidney Dis*. 2008;51:373–384.

36. de Jong PE, Verhave JC, Pinto-Sietsma SJ, et al. Obesity and target organ damage: the kidney. *Int J Obes Relat Metab Disord*. 2002;26(suppl 4):S21–S24.

37. Garland JS. Elevated body mass index as a risk factor for chronic kidney disease: current perspectives. *Diabetes Metab Syndr Obes*. 2014;7:347–355.

38. Nazare JA, Smith JD, Borel AL, et al. Ethnic influences on the relations between abdominal subcutaneous and visceral adiposity, liver fat, and cardiometabolic risk profile: the International Study of Prediction of Intra-Abdominal Adiposity and Its Relationship With Cardiometabolic Risk/Intra-Abdominal Adiposity. *Am J Clin Nutr*. 2012;96:714–726.

39. Xi B, Liang Y, He T, et al. Secular trends in the prevalence of general and abdominal obesity among Chinese adults, 1993-2009. *Obes Rev*. 2012;13:287–296.

40. Flegal KM CM, Ogden CL, Curtion LR. Prevalence and trends in obesity among US adults, 1999-2008. *JAMA*. 2010;303:235–2412.

41. National Bureau of Statistics of China. Beijing, China. 2015. Available at: http://www.stats.gov.cn/english/. Accessed July 20, 2015.

42. Wu X, Duan X, Gu D, et al. Prevalence of hypertension and its trends in Chinese populations. *Int J Cardiol*. 1995;52:39–44.

43. Pan XR, Yang WY, Li GW, et al. Prevalence of diabetes and its risk factors in China, 1994. National Diabetes Prevention and Control Cooperative Group. *Diabetes Care*. 1997;20:1664–1669.

44. Xu Y, Wang L, He J, et al. Prevalence and control of diabetes in Chinese adults. *JAMA*. 2013;310:948–959.

45. Hanevold CD, Pollock JS, Harshfield GA. Racial differences in microalbumin excretion in healthy adolescents. *Hypertension*. 2008;51:334–338.

46. Trachtenberg F, Barregard L. The effect of age, sex, and race on urinary markers of kidney damage in children. *Am J Kidney Dis*. 2007;50:938–945.

47. Kruzel-Davila EWW, Aviram S, Skorecki K. APOL1 nephrology:From gene to mechanisms of kidney injury. *Nephrol Dial Transplant*. 2016;31:349–358.

48. Haynes R, Staplin N, Emberson J, et al. Evaluating the contribution of the cause of kidney disease to prognosis in CKD: results from the Study of Heart and Renal Protection (SHARP). *Am J Kidney Dis*. 2014;64:40–48.

49. Soderland P, Lovekar S, Weiner DE, et al. Chronic kidney disease associated with environmental toxins and exposures. *Adv Chronic Kidney Dis*. 2010;17:254–264.

50. Kim NH, Hyun YY, Lee KB, et al. Environmental heavy metal exposure and chronic kidney disease in the general population. *J Korean Med Sci*. 2015;30:272–277.

51. Brook RD, Rajagopalan S, Pope CA 3rd, et al. Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association. *Circulation*. 2010;121:2331–2378.

52. Miller WG, Bruns DE, Hortin GL, et al. Current issues in measurement and reporting of urinary albumin excretion. *Clin Chem*. 2009;55:24–38.

53. Kidney Disease: Improving Global Outcomes Transplant Work G. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant*. 2009;9(suppl 3):S1–S155.