Prevalence of chronic kidney disease markers: Evidence from a three-million married population with fertility desire in rural China

Ye Du1, Shikun Zhang2, Mei Hu3, Qiaomei Wang2, Haiping Shen2, Yiping Zhang2, Donghai Yan2, Yuanyuan Li4, Man Zhang3 & Qun Meng1,5

We aimed to assess the prevalence of chronic kidney diseases (CKD) markers among the married residents with fertility desire in rural China. Demographic and clinical data were collected from the National Free Pre-Conception Health Examination Project. Estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m², proteinuria, and hematuria were defined as markers of CKD. GFR was evaluated by using serum creatinine level and the Asian-modified CKD epidemiology collaboration equation. Automated urine dry chemical and microscopic analyses were employed to identify proteinuria and hematuria. The prevalence of CKD markers was 2.92% in the 3,091,379 participants. eGFR < 60 mL/min/1.73 m², hematuria and proteinuria was observed in 0.85%, 1.41% and 0.71%, respectively. The prevalence of CKD markers varied greatly across different geographical locations, which was the highest in the Eastern Region (3.86%; 95% confidence interval [CI]: 3.81–3.91%), moderate in the Central Region (2.80%; 95% CI: 2.77–2.82%), and lowest in the Western Region (2.62%; 95% CI: 2.59–2.65%). Hypertension, obesity, positive hepatitis B virus surface antigen (HBsAg), age (increased by every 5 years), female gender, and living area were potential risk factors for CKD. In rural China, the prevalence of CKD markers in the married couples with fertility desire is low.

The research on chronic kidney disease (CKD) has drawn more and more attention in the field of public health across the world, since the prevalence of CKD has been estimated to be high in many countries and regions1–9. The outcomes of advanced CKD can be devastating in terms of serious complications, demands for renal replacement therapy and increased risk for cardiovascular diseases10–15. The cost for CKD diagnosis and therapy rose up to $50.4 billion in the U.S. Medicare system in 201316. The cost on CKD per capita per year was twice as high compared to the average Medicare patients17. CKD brings a heavy burden to patients and their families. Fortunately, CKD can be identified simply by blood and urine tests18. Timely diagnosis and treatment of CKD can help improve clinical outcome19.

According to Kidney Disease Improving Global Outcomes (KDIGO) Controversies Conference, the studies on CKD should include all ages and special populations18. In the past decade, research on CKD in China has been focused on urban residents20–25. In contrast, a very few study on CKD has been performed in rural areas, given China’s rural residents comprising 50.32% of its whole population26. Poverty and social deprivation are emerging as major risk factors for CKD in both developing and developed countries27. There has been accumulating evidence suggesting that prevalence of CKD may dramatically increase in those populations with low socioeconomic status (SES)28, 29. Living standard is relatively low in rural China due to dual economy. CKD in rural population of reproductive age has a heavy burden on their families and society.

1Department of Social Medicine and Health Management, Public Health College, Harbin Medical University, Harbin, China. 2Department of Maternal and Child Health, National Health and Family Planning Commission of the PRC, Beijing, China. 3Department of Clinical Laboratory, Beijing Shijitan Hospital, Capital Medical University, Beijing, China. 4Department of Maternal and Child Health Research, National Research Institute for Family Planning, Beijing, China. 5Department of Statistics and Information, National Health and Family Planning Commission of the PRC, Beijing, China. Ye Du and Shikun Zhang contributed equally to this work. Correspondence and requests for materials should be addressed to Q.M. (email: mengqun@moh.gov.cn)
The purpose of the current research is to evaluate the prevalence of CKD markers in the married couples with fertility desire across rural China, and to investigate variation in prevalence generated by age, gender, residential area, as well as common diseases including hypertension, obesity, diabetes and hepatitis B. The National Free Pre-Conception Health Examination Project (NFPHEP) has offered us a unique opportunity to explore the epidemiology of married population with fertility desire in rural China. NFPHEP provided free pre-conception health examinations for married couples across 31 provinces and regions in rural China in 2010, in an attempt to improve the level of childbearing.

**Methods**

**Design and participants.** This research has been approved by the Institutional Review Board of Chinese Association of Maternal and Child Health Studies. All methods were performed in accordance with the relevant guidelines and regulations. A population-based cross-sectional study was conducted on the basis of NFPHEP database from January 1, 2010 to December 31, 2012. The random cluster sampling was used in this study by counties. The target people in the selected counties were eligible to participate into the study. 220 counties were sampled randomly across 31 provinces and regions in China. All couples with a plan to get pregnant within the next 6 months registered and completed a standardized family healthcare file in the village-level family planning service offices. They accepted a free medical examination by qualified medical care personnel according to the unified specification in the county-level family planning service organization. Each participant had written informed consent before enrollment.

In order to assure the quality of examination, all the investigators and staff members had been well-trained on methodology and process. A manual of procedures was distributed to provide detailed instructions for how to administer questionnaires, test blood pressure, perform anthropometric measurements, as well as conduct biological specimen collection and transportation. With the assistance of trained local health staff, all participants had completed a standardized questionnaire including social and demographic status (age, gender, career, education and residential region), personal health history (e.g., hypertension and diabetes). The data were submitted to and double checked by NFPHEP quality inspection center once every month.

The mainland of China was divided into three regions based on the level of economic development, which were Eastern Region (coastal areas), Central Region (inland areas) and Western Region (remote areas). According to their residential areas, all participants were divided into three regional groups: Eastern Region (including Liaoning Province, Beijing Municipality, Tianjin Municipality, Hebei Province, Shandong Province, Jiangsu Province, Shanghai Municipality, Zhejiang Province, Fujian Province, Guangdong Province, and Hainan Province), Central Region (including Shanxi Province, Jilin Province, Heilongjiang Province, Anhui Province, Jiangxi Province, Henan Province, Hebei Province, and Hunan Province), and Western Region (including Inner Mongolia Autonomous Region, Chongqing Municipality, Guangxi Zhuang Autonomous Region, Sichuan Province, Guizhou Province, Yunnan Province, Tibet Autonomous Region, Shaanxi Province, Gansu Province, Qinghai Province, Ningxia Hui Autonomous Region, and Xinjiang Uygur Autonomous Region). The age of the enrolled population was ranged from 20 to 49 years.

**Screening Protocol and Evaluation Criteria.** According to the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guideline, estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m², proteinuria, and hematuria were defined as markers of CKD. As our study did not repeat the measurements until three months later, the chronicity criterion of CKD was not applied to this definition. The morning spot urine samples were collected to identify hematuria and proteinuria by means of automated urine dry chemical analysis. Samples with positive hematuria for one or more times were reexamined through microscopic analysis within 2 hours by qualified technicians in the county clinical laboratories. Presence of 3 or more red blood cells per high-power field was considered abnormal. Subjects with hematuria and pyuria were considered to have urinary tract infection and excluded from data analysis. Women undergoing menstruation were also excluded from urine analysis.

Blood samples were collected by means of venipuncture after an overnight fast of at least 10 hours and immediately sent to the county clinical laboratories. Fasting blood glucose (only for women), serum creatinine (Scr), and hepatitis B virus surface antigen (HBsAg) were examined by qualified technicians. The reagent kits approved by the China Food and Drug Administration were chosen by the local laboratories on their preference, and were double checked by National Center of Clinical Laboratories for Quality Inspection (NCCLQI). Sensitivity, specificity, and value of the selected reagents from all the involved county laboratories were higher than 95%. Provincial Center of Clinical Laboratories for Quality Inspection carried out casual inspections and NCCLQTD conducted an external quality assessment (EQA) for quality control.

Serum creatinine was measured by enzymatic method with Enzymatic Creatinine-2 Reagents (Siemens Healthcare Diagnostics Inc.) and isotope dilution mass spectrometry (IDMS) method as the reference standard. Hepatitis B virus surface antigen (HBsAg) was detected by Siemens ADVIA 2400 Chemistry System with reagents produced by Abbott (Abbott Park, IL, USA) as the reference standard. eGFR was calculated by using Chinese modification of diet in renal disease (C-MDRD) equation and Asian-modified chronic kidney disease epidemiology collaboration (CKD-EPI) equation, respectively as follows:

\[ C\text{-MDRD: } eGFR (mL/min /1.73 m^2) = 175 \times \frac{Scr (mg/dl)}{1.234^{1.234} \times age (years)^{-0.179} \times [female \times 0.79]}; \]
Asian-modified CKD-EPI equation: \[ eGFR(\text{mL/min} / 1.73\, \text{m}^2) = 151 \times (0.993)^{\text{BMI}} \times \frac{\text{Scr}}{0.7}^{0.328} \text{ (female: if Scr } \leq 0.7 \, \text{mg/dl)}}; 151 \times (0.993)^{\text{BMI}} \times \frac{\text{Scr}}{0.7}^{1.210} \text{ (female: if Scr } > 0.7 \, \text{mg/dl)}}; 149 \times (0.993)^{\text{BMI}} \times \frac{\text{Scr}}{0.9}^{0.412} \text{ (male: if Scr } \leq 0.9 \, \text{mg/dl)}}; 149 \times (0.993)^{\text{BMI}} \times \frac{\text{Scr}}{0.9}^{1.210} \text{ (male: if Scr } > 0.9 \, \text{mg/dl)}}.

We adopted Asian-modified CKD-EPI equation to evaluate CKD prevalence.

Arterial blood pressure was measured in sitting position by sphygmomanometer three times at 5 minute intervals after the subjects had rested for at least 15 minutes. The mean of the three readings was calculated unless the difference between readings was greater than 10 mmHg, in which case the mean of the two closest readings was applied. Hypertension was defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, or by any self-reported history of hypertension. Because fasting blood glucose and postprandial blood glucose of the men were not measured, for men, “diabetes” was defined as history of diabetes. For women, diabetes was defined as history of diabetes or fasting blood glucose ≥ 7.0 mmol/L. The body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. According to Chinese criteria of weight for adults, 18.5 kg/m² was in normal range, BMI < 18.5 kg/m² represented underweight, 24.0 kg/m² ≤ BMI < 28.0 kg/m² represented overweight. Obesity was defined as BMI ≥ 28.0 kg/m².

### Statistical analysis
Continuous variables were analyzed by one-way ANOVA. Categorical variables were analyzed by χ² test. The prevalence of CKD markers, eGFR < 60 mL/min/1.73 m², hypertension, and proteinuria were analyzed with age groups by spearman correlation test. To investigate the risk factors and indicators for CKD, logistic regression models were applied. The crude and multivariable adjusted odds ratios (ORs) were reported. Covariates included in the multivariable logistic regression models were hypertension (no vs. yes), obesity (no vs. yes), HBsAg positive (no vs. yes), gender (female vs. male), and region (eastern region: 0; central region: 1; and western region: 2). Age was defined as categorical variable with a 5-year interval, and 20–24 years was treated as a dummy variable in the Logistic Regression Model. All statistical data were analyzed after removing the missing items. The significant level was 0.05 and all of the analyses were two-sided tests. Statistical analyses were performed with SPSS version 21.0.

### Results
#### Demographic and clinical characteristics of the studied population
3,091,379 participants filled in the questionnaire. Rate of loss of participants due to uncompleted blood test and urinalysis was 3.58%, 0.51% and 3.2%, respectively, in the Eastern Region, Central Region and Western Region. The average age was 27.04 ± 7.10 (standard deviation [SD]) years. As shown in Table 2, the proportion of female was 51.70%. The surveyed population mainly engaged in agriculture. Nearly 2/3 of people had junior middle-school education. The average level of Scr was 77.06 ± 20.35 μmol/L. 4.06% of the population was suffering from hypertension, with males more susceptible than females. More females had a history of diabetes than males (0.0214% vs. 0.0156%). The prevalence of diabetes was 1.41% for females. 5.64% of the population had positive HBsAg, with males more susceptible than females. The prevalence of underweight in females was 3 times higher than that in males, while the prevalence of overweight and obesity in males was twice as that in females.

The prevalence of CKD markers by Asian-modified CKD-EPI equation for eGFR was 2.92% in the surveyed population (1.81% and 3.95%, respectively, in males and females). If hematuria was excluded, the prevalence of CKD markers was dropped to 1.54% (1.08% and 1.96%, respectively, in males and females). By adopting Asian-modified CKD-EPI equation for eGFR, the prevalence of eGFR below 60 mL/min/1.73 m² was 0.85% (0.43% and 1.24% in males and females, respectively). By adopting C-MDRD formula, the prevalence of eGFR below 60 mL/min/1.73 m² was 1.50% (0.98% and 1.91% in males and females, respectively). The prevalence of hematuria was 1.41% (2.03% vs. 0.74% in females vs. males). The prevalence of proteinuria was 0.71% (0.74% vs. 0.66% in females vs. males).

#### The prevalence of CKD stages
As shown in Table 2, the prevalence of CKD 1–5 stage based on the estimated GFR by Asian-modified CKD-EPI equation were 1.66%, 0.40%, 0.79%, 0.03% and 0.03% respectively. There were differences between the prevalence of the males and the females in every CKD stage.

#### The prevalence of CKD markers in different geographical locations
As shown in Table 3, the prevalence of CKD markers varied greatly due to different geographical locations, which was the highest in the Eastern Region (3.86%), moderate in the Central Region (2.80%) and the lowest in the Western Region (2.62%). The prevalence of hematuria and proteinuria in Eastern Region was significantly higher than that in the Central and Western regions. Hypertension, obesity and positive HBsAg were most frequently observed in the Eastern Region.

#### The prevalence of CKD markers in different age groups
As shown in Fig. 1, the prevalence of CKD markers except proteinuria increased with age. The prevalence of CKD markers in the aged 46–49 group was two times higher than that in the aged 20–25 group. The prevalence of eGFR below 60 mL/min/1.73 m² (by Asian-modified CKD-EPI equation) in the aged 46–49 group was four times higher than that in the aged 20–25 group.
The prevalence of CKD markers in the population with chronic diseases. As shown in Table 4, the prevalence of CKD markers was significantly higher in subjects with hypertension, diabetes, positive HBsAg, and obesity compared to their counterparts.

The risk factors for CKD and indicators. Table 5 listed the crude and adjusted odds ratios (ORs) for CKD as well as potential indicators. Hypertension, obesity, positive HBsAg, and age (increased by every 5 years) were independent risk factors for eGFR < 60 mL/min/1.73 m². Hypertension, obesity, positive HBsAg, female, age (increased by every 5 years) and region were independent risk factors for hematuria. Independent risk factors for proteinuria included hypertension, obesity, positive HBsAg, female and region. Hypertension, obesity, positive HBsAg, female, age (increased by every 5 years) and region were independent risk factors for CKD.

Table 1. Sociodemographic and clinical characteristics of the married population with fertility desire in rural China. CKD: chronic kidney disease. eGFR: estimated glomerular filtration rate. HBsAg: hepatitis B virus surface antigen. BMI: body-mass index. C-MDRD equation: Chinese modification of diet in renal disease equation. CKD-EPI equation: chronic kidney disease epidemiology collaboration equation. SD: standard deviation.
Discussion

This study of three-million participants provides important information on CKD in rural China and fills the gap in knowledge. The prevalence of CKD markers (2.92%) among married population with fertility desire in rural China is markedly lower than the average national level in Mainland China (10.8%) and in Taiwan (11.93%)\(^5,22\). A higher prevalence of CKD markers in the developed Eastern Region is different from other studies in which the prevalence of CKD was higher in people with low socioeconomic status. The factors below may account for the difference. First, age variation exists in the studies. The average age in this study, in Mainland China and in Taiwan was 27.04 ± 7.10, 49.6 ± 15.2, and 41.8 ± 14.1 years, respectively\(^5,22\). Age is an independent risk factor for CKD.

### Table 2. Prevalence of CKD stages according to the eGFR in the married population with fertility desire in rural China by gender. CKD: chronic kidney disease. eGFR: estimated glomerular filtration rate. CKD-EPI equation: chronic kidney disease epidemiology collaboration equation.

| CKD stage | Total (n, %) | Male (n, %) | Female (n, %) | P-value |
|-----------|-------------|-------------|---------------|---------|
| 1         | 51428 (1.66) | 17766 (1.19) | 33662 (2.11) | <0.001  |
| 2         | 12513 (0.40) | 2820 (0.19)  | 9693 (0.61)  | <0.001  |
| 3         | 24508 (0.79) | 5669 (0.38)  | 18839 (1.18) | <0.001  |
| 3a        | 21235 (0.68) | 4512 (0.30)  | 16723 (1.05) | <0.001  |
| 3b        | 3273 (0.11)  | 1157 (0.08)  | 2116 (0.13)  | <0.001  |
| 4         | 794 (0.03)   | 416 (0.03)   | 378 (0.02)   | <0.001  |
| 5         | 872 (0.03)   | 325 (0.02)   | 547 (0.03)   | <0.001  |

### Table 3. Prevalence of and risk factors for CKD in the married population with fertility desire by regions in rural China. Data are represented as n (%), % (95% CI), or mean ± SD. BMI: body-mass index. CKD: chronic kidney disease. EGFR: estimated glomerular filtration rate. CKD-EPI equation: chronic kidney disease epidemiology collaboration equation. Obesity: BMI ≥ 28 (kg/m²). HBsAg: hepatitis B virus surface antigen. SD: standard deviation. CI: confidence interval.

| Region        | Participants (n, %) | Women (n, %) | Age (years, mean ± SD) | BMI (kg/m², mean ± SD) | CKD markers (by Asian modified CKD-EPI equation, %) | EGFR < 60 mL/min/1.73 m² (by Asian modified CKD-EPI equation, %) | Hematuria (%) | Proteinuria (%) | Hypertension (%) | Diabetes (%) | Obesity (%) | HBsAg positive (%) |
|---------------|---------------------|--------------|------------------------|------------------------|------------------------------------------------|------------------------------------------------|----------------|----------------|-----------------|--------------|--------------|-------------------|
| Eastern region | 513318 (16.60)      | 270297 (52.66) | 27.74 ± 5.05           | 22.10 ± 4.06           | 3.86 (3.81–3.91)                                   | 0.85 (0.83–0.88)                                      | 2.31 (2.27–2.35) | 0.82 (0.79–0.84) | 6.78 (6.71–6.85)   | 0.71 (0.69–0.74) | 5.23 (5.17–5.29) | 6.56 (6.49–6.63)   |
| Central region | 1521785 (49.23)     | 785916 (51.64) | 26.77 ± 8.61           | 21.88 ± 3.41           | 2.80 (2.77–2.82)                                   | 0.89 (0.88–0.91)                                      | 1.29 (1.27–1.31) | 0.64 (0.63–0.65) | 3.40 (3.37–3.43)   | 0.87 (0.85–0.88) | 3.09 (3.06–3.11) | 5.55 (5.51–5.58)   |
| Western region | 1056276 (34.17)     | 541892 (51.30) | 27.10 ± 5.29           | 21.86 ± 4.40           | 2.62 (2.59–2.65)                                   | 0.78 (0.77–0.80)                                      | 1.14 (1.12–1.16) | 0.75 (0.73–0.77) | 3.83 (3.79–3.86)   | 0.56 (0.54–0.57) | 3.12 (3.09–3.15) | 5.39 (5.35–5.43)   |

### Figure 1. The prevalence of CKD indicators in the married population with fertility desire by age-groups in rural China.
Hepatitis B virus (HBV) infection is highly endemic in rural China. Several studies have revealed a strong association of CKD with increased morbidity and mortality of hepatitis B. At present, the studies on risk factors for CKD in China seldom involve HBV infection. We found that the prevalence of CKD markers is higher in the participants with positive HBsAg than those with negative HBsAg; and importantly, positive HBsAg is an independent risk factor for CKD. The result informs that universal hepatitis B vaccination program for infants enacted in 1992 to control HBV infection might also be beneficial in controlling CKD in China.

Table 4. The prevalence of CKD indicators of the married population with fertility desire by chronic diseases in rural China. Data are represented as % (95% CI). CKD: chronic kidney disease. EGFR: estimated glomerular filtration rate. Obesity: body-mass index ≥28 (kg/m²). HBsAg: hepatitis B virus surface antigen. CI: confidence interval.

| CKD markers | eGFR < 60 mL/min/1.73 m² | Hematuria | Proteinuria |
|-------------|--------------------------|-----------|-------------|
| Hypertension (%) | | | |
| No | 2.87 (2.85–2.89) | 0.84 (0.82–0.85) | 1.38 (1.36–1.39) | 0.67 (0.66–0.68) |
| Yes | 4.62 (4.51–4.74) | 1.17 (1.11–1.23) | 2.06 (1.98–2.14) | 1.45 (1.39–1.52) |
| p | <0.001 | <0.001 | <0.001 | <0.001 |
| Diabetes (%) | | | |
| No | 2.91 (2.89–2.93) | 0.83 (0.82–0.84) | 1.40 (1.39–1.41) | 0.70 (0.69–0.71) |
| Yes | 6.59 (6.26–6.91) | 2.80 (2.58–3.02) | 2.34 (2.14–2.53) | 1.55 (1.39–1.71) |
| p | <0.001 | <0.001 | <0.001 | <0.001 |
| HBsAg positive (%) | | | |
| No | 2.91 (2.89–2.92) | 0.84 (0.83–0.85) | 1.39 (1.38–1.41) | 0.73 (0.72–0.75) |
| Yes | 3.57 (3.48–3.66) | 1.08 (1.03–1.12) | 1.66 (1.59–1.72) | 1.51 (1.35–1.67) |
| p | <0.001 | <0.001 | <0.001 | <0.001 |
| Obesity (%) | | | |
| No | 2.90 (2.89–2.92) | 0.84 (0.83–0.85) | 1.40 (1.38–1.41) | 0.66 (0.65–0.67) |
| Yes | 4.14 (4.02–4.26) | 1.02 (0.96–1.08) | 1.76 (1.68–1.84) | 5.63 (2.63–8.62) |
| p | <0.001 | <0.001 | <0.001 | <0.001 |
| OR (crude) | OR (adjusted) |
|-----------|--------------|
| **CKD** | **eGFR < 60 mL/min/1.73 m²** | **Hematuria** | **Proteinuria** | **eGFR < 60 mL/min/1.73 m²** | **Hematuria** | **Proteinuria** |
| Hypertension | 1.36 (1.31–1.40) | 1.41 (1.34–1.48) | 1.51 (1.45–1.57) | 2.17 (2.07–2.28) | 1.63 (1.59–1.68) | 1.36 (1.28–1.43) | 1.55 (1.49–1.62) | 2.04 (1.94–2.14) |
| Obesity | 1.13 (1.08–1.17) | 1.21 (1.14–1.29) | 1.26 (1.21–1.33) | 2.06 (1.96–2.18) | 1.42 (1.37–1.46) | 1.20 (1.13–1.27) | 1.28 (1.22–1.34) | 1.87 (1.77–1.98) |
| HBsAg positive | 1.13 (1.10–1.17) | 1.29 (1.23–1.35) | 1.19 (1.15–1.24) | 1.24 (1.18–1.31) | 1.27 (1.24–1.31) | 1.35 (1.29–1.42) | 1.23 (1.19–1.28) | 1.24 (1.18–1.31) |
| Female | 9.53 (9.29–9.78) | 2.92 (2.82–2.99) | 2.79 (2.73–2.85) | 1.13 (1.10–1.16) | 2.44 (2.41–2.48) | 3.40 (3.30–3.50) | 3.00 (2.93–3.07) | 1.16 (1.13–1.19) |

**Table 5.** Risk factors for CKD and indicators of married population with fertility desire in rural China. Data are represented as odds ratio (95% CI). CKD: chronic kidney disease. eGFR: estimated glomerular filtration rate (by Asian modified CKD-EPI equation). Obesity: body-mass index ≥ 28 (kg/m²). HBsAg: hepatitis B virus surface antigen. CI: confidence interval.

The prevalence of CKD in men was also higher than that in women. In our study, the incidence of hypertension, obesity, and HBV infection, as well as the mean age of females were all lower than those of males, but the prevalence of CKD markers in females was as 2 times as that in males. After hematuria was excluded from the definition of CKD, the prevalence CKD markers in females remained much higher than that in males. Different congenital susceptibility to kidney damage may contribute to different prevalence of CKD markers between males and females.

This study has some limitations. First of all, according to KDIGO guideline, CKD should have indicators of kidney damage over three months. In this research, all the indicators of CKD were tested from single measurement, because it was extremely difficult to conduct repeated examination in such a large-scale investigation. Lack of confirmatory dipstick urinalysis and demonstrated chronicity of eGFR below 60 mL/min/1.73 m² may lead to remarkably overrated CKD prevalence. Although some authors would believe that most of the previous studies using single measurement for serum creatinine and dipstick urinalysis might have been equally affected, this limitation would result in variation in prevalence of CKD across studies. The actual prevalence of CKD in married population with fertility desire in rural China would be even lower than that in our study. Second, applying dipstick urinalysis as screening experiment might have missed diagnosis of kidney damage, thus underestimating the prevalence of CKD. However, in the nationwide investigation, dipstick urinalysis has been used as the most convenient, feasible and cost-effective tool to identify kidney damage, especially in rural areas. Dipstick urinalysis is sensitive enough to detect urinary protein equivalent to microalbuminuria. Glomerulonephritis remains the most common chronic kidney disease and the leading cause of end-stage renal disease in China. So dipstick urinalysis, rather than urinary albumin to creatinine ratio, was selected to diagnose hematuria and proteinuria. The higher prevalence of hematuria among young women might be from renal or urological origin, but not necessarily caused by CKD, which requires further investigation. Third, there was possible potential selection bias that would underestimate the prevalence of CKD. The population with serious CKD might not enroll in the survey because of having no fertility desire. Unmarried people in rural China were not included, which might be another major limitation in the current research. Forth, fasting blood glucose was measured only for women, which was another major limitation. The association of diabetes with CKD prevalence stratified by gender requires further investigation.

Despite the limitations, with random sampling and a 3-million sample size, this study had a high power that the power of CKD markers (by Asian modified CKD-EPI equation) and proteinuria (by Asian modified CKD-EPI equation and excluding hematuria) between males and female was 100%. For the first time, our study has reported the prevalence of CKD markers in married population with the mean age of 27 years in rural China. Our study also highlights variation in the prevalence of CKD across regions and potential factors attributed to this variation. Different from rural China, the prevalence of CKD markers in married population with fertility desire is low. However, in the developed Eastern Region, the prevalence of CKD markers is observed in the developed Eastern Region. Hypertension, obesity, positive HBsAg, female, age and living area were independent risk factors for CKD. These results indicate that economic development and changing life style have affected the epidemiology of CKD. Better understanding and management of risk factors for CKD is critical to prevent this disease.
References
1. Coren, J. et al. Prevalence of chronic kidney disease in the United States. *Jama* 298, 2038–2047, doi:10.1001/jama.298.17.2038 (2007).
2. Chadban, S. J. et al. Prevalence of kidney damage in Australian adults: The AusDiab kidney study. *Journal of the American Society of Nephrology* JASN 14, S131–138 (2003).
3. Cepoi, V., Onofriescu, M., Segall, L. & Covic, A. The prevalence of chronic kidney disease in the general population in Romania: a study on 60,000 persons. *International urology and nephrology* 44, 213–220, doi:10.1007/s11255-011-9923-9 (2012).
4. Ohno, Y. et al. Prevalence of and factors associated with chronic kidney disease (CKD) in Japanese subjects with not all chronic diseases, undergoing an annual health checkup. *Kidney & blood pressure research* 36, 139–148, doi:10.1159/000341490 (2012).
5. Wen, C. P. et al. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. *Lancet (London, England)* 371, 2173–2182, doi:10.1016/s0140-6736(08)60952-6 (2008).
6. Li, P. K. et al. Prevalence of silent kidney disease in Hong Kong: the screening for Hong Kong Asymptomatic Renal Population and Evaluation (SHARE) program. *Kidney international. Supplement* S56–40, doi:10.1111/j.1523-1755.2005.09410.x (2005).
7. Hooi, L. S. et al. A population-based study measuring the prevalence of chronic kidney disease among adults in West Malaysia. *Kidney international* 84, 1034–1040, doi:10.1038/ki.2013.220 (2013).
8. Mills, K. T. et al. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney international* 88, 950–957, doi:10.1038/ki.2013.230 (2015).
9. Perkovic, V. et al. High prevalence of chronic kidney disease in Thailand. *Kidney international* 73, 473–479, doi:10.1038/ki.2008.492 (2008).
10. Bello, A. K., Nnawko, E. & El Nahas, A. M. Prevention of chronic kidney disease: a global challenge. *Kidney international. Supplement* SI1–17, doi:10.1111/j.1523-1755.2005.09802.x (2005).
11. Matsushita, K. et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet (London, England)* 375, 2073–2081, doi:10.1016/S0140-6736(10)60674-5 (2010).
12. Kasiske, B. L. & Eckardt, K. U. Chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. *Kidney international* 72, 247–259, doi:10.1038/sj.ki.5002345 (2007).
13. Hallan, S. I. et al. International comparison of the relationship of chronic kidney disease prevalence and ESRD risk. *Journal of the American Society of Nephrology: JASN* 17, 2275–2284, doi:10.1681/asn.2005121273 (2006).
14. Zhang, L. et al. Community-based screening for chronic kidney disease among populations older than 40 years in Beijing. *Nephrology, dialysis, transplantion: official publication of the European Dialysis and Transplant Association - European Renal Association* 22, 1093–1099, doi:10.1093/ndt/gfl763 (2007).
15. Zhang, L. et al. Prevalence and factors associated with CKD: a population study from Beijing. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 51, 373–384, doi:10.1053/ajkd.2007.11.009 (2008).
16. Zhang, L. et al. Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet (London, England)* 379, 815–822, doi:10.1016/s0140-6736(12)60033-6 (2012).
17. Chen, W. et al. Prevalence and risk factors associated with chronic kidney disease in an adult population from southern China. *Nephrology, dialysis, transplantion: official publication of the European Dialysis and Transplant Association - European Renal Association* 24, 1205–1212, doi:10.1093/ndt/gfn604 (2009).
18. Chen, N. et al. Community-based study on CKD subjects and the associated risk factors. *Nephrology, dialysis, transplantion: official publication of the European Dialysis and Transplant Association - European Renal Association* 21, 2117–2123, doi:10.1093/ndt/gfn767 (2009).
19. Guo, Z. W., Q. Epidemiologic investigation of chronic kidney disease in Chengdu urban population. *Chin J Nephrol.* 28, 444–449 (2012).
20. National Bureau of Statistics, PRC. The sixth National Census. http://www.stats.gov.cn/tjsj/tjgb/rkpcgb/qgrkpcgb/20110428_30327.html (2011).
21. Hossain, M. P., Goyder, E. C., Rigby, J. E. & El Nahas, M. CKD and poverty: a growing global challenge. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 53, 166–174, doi:10.1016/j.jnkf.2007.10.007 (2009).
22. Zhang, S. K. et al. The significance, design and implement of the National Free Pre-conception Health Examination Project in China. *Natl Med J China.* 95, 162–165 (2015).
23. Ministry of Health, PRC. *China Health Statistics Yearbook 2013* (ed. Peking Union Medical College Press. Inc.) 2–3 (Beijing, 2010).
24. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 39, S1–266 (2002).
25. Wang, Q. M. et al. To establish the system of quality assurance on the physical examination of the National Free Pre-conception Health Examination Project. *Natl Med J China.* 95, 166–168 (2015).
26. Ma, Y. C. et al. Modified glomerular filtration rate estimating equation for Chinese patients with chronic kidney disease. *Journal of the American Society of Nephrology: JASN* 17, 2937–2944, doi:10.1681/asn.2006040368 (2006).
27. Stevens, L. A. et al. Evaluation of the Chronic Kidney Disease Epidemiology Collaboration equation for estimating the glomerular filtration rate in multiple ethnicities. *Kidney international* 79, 555–562, doi:10.1038/ki.2010.462 (2011).
28. National Health and Family Planning Commission, PRC. *BMI Industry standard of the people’s Republic of China WS/T 428-2013: criteria of weight for adults* (ed. National Health and Family Planning Commission, PRC.) 1–2 (Beijing, 2013).
29. Levey, A. S. & Stevens, L. A. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. *American journal of kidney diseases: the official journal of the National Kidney Foundation* 55, 622–627, doi:10.1053/j.ajkd.2010.02.337 (2010).
30. Levey, A. S. et al. A new equation to estimate glomerular filtration rate. *Annals of internal medicine* 150, 604–612 (2009).
31. Du, X. et al. Implication of CKD-EPI equation to estimate glomerular filtration rate in Chinese patients with chronic kidney disease. *Renal failure* 33, 859–865, doi:10.3109/0886022X.2011.605533 (2011).
32. Du, X. et al. Is the Chronic Kidney Disease Epidemiology Collaboration four-level race equation better than the cystatin C equation? *Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association* 44, 2275–2284, doi:10.1016/s0140-6736(16)30033-6 (2012).
39. Kitiyakara, C. et al. The impact of different GFR estimating equations on the prevalence of CKD and risk groups in a Southeast Asian cohort using the new KDIGO guidelines. *BMC Nephrology* **13**, 1, doi:10.1186/1471-2369-13-1 (2012).

40. Liu, J. et al. Seroepidemiology of hepatitis B virus infection in 2 million men aged 21–49 years in rural China: a population-based, cross-sectional study. *The Lancet. Infectious diseases* **16**, 80–86, doi:10.1016/s1473-3099(15)00218-2 (2016).

41. Dan, F. S. Research on the differences of the development of well-off society in eastern, central and western region of China. *Research World* 2, 8–13 (2014).

42. Benghanem Gharbi, M. et al. Chronic kidney disease, hypertension, diabetes, and obesity in the adult population of Morocco: how to avoid "over"- and "under"-diagnosis of CKD. *Kidney International* **89**, 1363–1371, doi:10.1016/j.kint.2016.02.019 (2016).

43. Bruck, K. et al. CKD Prevalence Varies across the European General Population. *Journal of the American Society of Nephrology: JASN* **27**, 2135–2147, doi:10.1681 ASN.2015050542 (2016).

44. Huang, Y. P. et al. Community-based study on adult chronic kidney diseases and its associated risk factors in Shanghai. *Chin J Nephrol.* **24**, 872–876 (2008).

45. Hoy, W. E. et al. CKD in Aboriginal Australians. *American Journal of Kidney Diseases: The Official Journal of the National Kidney Foundation* **56**, 983–993, doi:10.1053/j.ajkd.2010.05.010 (2010).

46. Dialysis and Transplantation Registration Group. The report about the registration of dialysis and transplantation in China 1999. *Chin J Nephrol.* **17**, 77–78 (2001).

47. Konta, T. et al. Clinical utility of trace proteinuria for microalbuminuria screening in the general population. *Clinical and Experimental Nephrology* **11**, 51–55, doi:10.1007/s10157-006-0458-z (2007).

Acknowledgements
We sincerely thank all the health workers in the 31 provinces in China, the Center for Clinical Laboratory, especially in Beijing Shijitan Hospital, Capital Medical University for their great effort on NFPHEP. This study was supported by Beijing Municipal Administration of Hospitals’ Ascent Plan (DFL20150701). The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Author Contributions
Y.D. and S.Z. designed the study, analyzed the data, interpreted the results, and drafted the manuscript. M.H., Q.W., H.S., M.Z., Y.Z., D.Y., and Y.L. conducted the experiments and collected the data. Q.M. conceived, designed and supervised the study. Y.D. and M.Z. interpreted the results and performed statistical analysis. All authors participated in preparation of the manuscript.

Additional Information
Competing Interests: The authors declare that they have no competing interests.

Publisher’s note: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.

© The Author(s) 2017