Prevalence of chronic kidney diseases and its determinants among perimenopausal women in a rural area of North India: A community-based study

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ABSTRACT

The burden of noncommunicable diseases is rising in India. A high prevalence of lifestyle-related diseases in perimenopausal women in the community makes them vulnerable to chronic kidney diseases (CKD). A cross-sectional community-based study was carried out among women >35 years of age in the village of Ballabgarh, Haryana (north India). Eligible women were selected by the probability proportionate to size sampling method. Estimation of glomerular filtration rate (GFR) was carried out by using the age- and body surface area (BSA)-adjusted Cockcroft–Gault (CG) and modification of diet in renal disease (MDRD) equations. Association of risk factors such as obesity, hyperlipidemia, hypertension, and diabetes mellitus with CKD was also assessed using multivariate logistic regression analysis. A total of 455 women were studied. The prevalence of low GFR (<60 mL/min/1.73 m^2) by the CG/BSA equations and MDRD equation was found to be 18.2% (95% confidence interval 14.6, 21.8) and 5.9% (95% confidence interval 3.7, 8.1), respectively. Obesity (odds ratio 15.5) ($P = 0.002$), hyperlipidemia (odds ratio: 2.5) ($P = 0.017$), and age ($P < 0.001$) were significantly associated with reduced GFR on multivariate logistic regression analysis. This study observed a high prevalence of CKD and its risk factors among perimenopausal women in a rural community in north India. The study highlights the need of a multipronged, community-based intervention strategy that includes a high-risk screening approach and awareness generation about CKD and its risk factors in the community.

Key words: Chronic kidney disease, India, perimenopausal women, prevalence

Introduction

Chronic kidney disease (CKD) is defined as either structural and/or functional abnormality of the kidney or reduced glomerular filtration rate (GFR) to a level less than 60 mL/min/1.73 m^2. CKD has become an important public health problem not only because the number of patients with end-stage renal disease (ESRD) is steadily increasing worldwide, but also because it has been documented as a significant risk factor for cardiovascular disease (CVD).[1-5]

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In the last few decades, there has been an increase in the noncommunicable diseases burden in India. This change in the public health scenario might be attributed to lifestyle (habit) changes occurring along with economic development. India, often referred to as the diabetes capital of the world, also showed increasing trends with the obese population.[6] According to the CURES cohort, every fifth person in India is suffering from hypertension.[7] Because of the presence of a high burden of risk factors, CKD may become a major public health problem in India in the near future.

Women constitute nearly half of the population in India. They have higher chances of development of risk factors of CKD such as obesity and hypertension, particularly in the perimenopausal period, compared with men.[8,9] GFR decreases with age, and CKD is more common in the later stage of life. Possible factors involved in the development of CKD are hypertension, impaired glucose tolerance or diabetes mellitus, dyslipidemia, and obesity, besides aging.[10-17]

Early identification and management of patients with mild renal disease and its risk factor have been recognized as an important strategy to delay the progression of renal disease and modification of risk factors.[18-22]

Only few community-based studies documenting the prevalence of CKD among perimenopausal women in rural India are found.[23,24] One study has used serum creatinine for the diagnosis of CKD.[23] It has been documented that screening by serum creatinine underestimates the CKD compared with the age- and body surface area (BSA)-adjusted Cockcroft–Gault (CG) and modification of diet in renal disease (MDRD) equations.

This study is part of a multisite intervention study.[25] In this study, we have estimated the prevalence of reduced GFR using both CG/BSA and MDRD equations. We also studied the association of various risk factors for CKD with reduced GFR among rural women.

Materials and Methods

This study was part of a multicentric community-based intervention study carried out in 2005-2008.[25] This study was conducted in villages under the Comprehensive Rural Health Services Project (CRHSP), Ballabgarh, Haryana, under All India Institute of Medical Sciences, New Delhi. Out of f the 28 villages in the project area, five villages were selected randomly. In these selected villages, 600 women (>35 years old) were selected by the probability proportional to size sampling method. Details of the sampling methodology are mentioned elsewhere.[25]

A prestructured, validated questionnaire was administered to all eligible women (who gave consent for blood investigation) seeking information about their demographic characteristics. Anthropometric measurements such as weight, height, waist circumference (WC), and calf circumference were recorded according to the standard guidelines. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by using a mercury sphygmomanometer (Diamond, Pune, Maharashtra, India). Two readings at an interval of 5 min were taken. If the difference of the two readings was more than 10 mm, a third reading was taken. The mean of the two readings was taken as the final reading. If the BP was found to be abnormal, a repeat measurement was done after 30 min.

Blood sample collection and laboratory investigations

Blood samples were drawn after obtaining written informed consent from the study participants. After overnight fasting, 5 ml of blood was taken from the antecubital vein, observing universal precautions. The collected blood samples were immediately transported to the laboratory at CRHSP, Ballabgarh, for fasting blood glucose (FBS), serum creatinine, serum urea, and blood cholesterol analysis. All biochemical investigations were carried out using a fully automatic autoanalyzer (ECO, Firmware version 3.1, UK). All samples were analyzed in the same laboratory on the same equipment throughout the duration of the study, with twice-daily quality control checks.

Operational definitions

Renal impairment

GFR was estimated using the CG equation corrected for gender and BSA, and MDRD equation. In this study, CG–GFR estimates were preferred over CG–creatinine clearance estimates, as the CG–GFR equation was likely to be more suitable for estimating subnormal GFR in the Indian population and, also, it corrects for renal tubular secretion of creatinine.[26]

CG/BSA equation:

$$\text{Creatinine clearance (mL/min/1.73 m}^2) = [(140 - \text{age}) \times (\text{weight})/(\text{serum creatinine} \times 72 \times \text{BSA}/1.73)] \times (0.85 \text{ for female}). \quad (1)$$

$$\text{BSA (m}^2) = 0.20247 \times (\text{height in meters})\ 0.725 \times (\text{weight in kg})\ 0.425$$

$$\text{CG–GFR estimate (mL/min/1.73 m}^2) = 0.84 \times (\text{creatinine clearance by equation 1})$$

MDRD equation:

$$\text{MDRD–GFR (mL/min/1.73 m}^2) = 186 \times (\text{serum creatinine}) - 1.154 \times (\text{age}) - 0.203 \times (0.742 \text{ for female}). \quad (2)$$

The estimated GFR (eGFR) was then used to classify subjects into Kidney Disease Outcomes Quality Initiative (K/DOQI) stages of CKD.[1] Renal impairment was defined as eGFR less than 60 mL/min/1.73 m^2. Thus, stages 3, 4, and 5 of K/DOQI were grouped as renal impairment.

Hypertension

Hypertension was defined as SBP ≥140 mmHg and DBP ≥90 mmHg as per the JNC-7 guidelines.[27] Patients taking antihypertensive drugs were also classified as hypertensive, even if their BP values were lower than the cutoffs. However, no adjustments in the cut-off values were made for diabetic status.

Diabetes mellitus

A known diabetic patient on treatment was considered diabetic, regardless of their glycemic control. For others, a 12-h fasting blood sugar level of ≥126 mg/dL was used as the cutoff for the diagnosis of diabetes.[28]

Obesity

Weight (in kg) and height (in m) were used to calculate body mass index (BMI). BMI was classified according to the WHO classification, with BMI ≥25 kg/m² as the cutoff for obesity.[29,30] Additionally, WC was used to assess body fat distribution. WC was measured as the smallest circumference between the lower ribs and the iliac crests. The mean of the two measurements was taken as the final, and a cut-off value of >80 cm was used for obesity.[30]

Statistical analysis

Results were expressed as absolute numbers, proportions, and means with standard deviations. Categorical variables were analyzed for associations by Chi-square test, and crude (unadjusted) odds ratio was calculated. Quantitative variables were analyzed using the *t*-test for normally distributed variables. Multivariate logistic regression models were framed, adjusting for all variables and significant two-way interactions between variables. All statistical tests were performed using SPSS software (SPSS Inc., Chicago, IL, USA; version 13). Confidence level was kept at 95% and $P < 0.05$ was taken as significant.

Ethical issues

Informed written consent was obtained from each study participant. Ethical clearance for the study was obtained from the Ethical Committee of the All India Institute of Medical Sciences, New Delhi.

Results

A total of 600 women were approached for participation in this study. Of these 600 women, 145 (24.2%) refused to give consent for clinical examination and/or blood investigation. The final sample achieved was 455 women. The age of the study participants was 45.2±8.4 years and the BMI was 22.2±5.2 kg/m². Serum creatinine was 0.68±0.24 mg/dl and urea was 26.9±8.1 mg/dl among the study population. Mean estimated GFR was 93.1±35.8 mL/min/1.73 m² by the CG/BSA equation and 111.9±35.7 mL/min/1.73 m² by the MDRD equation among the study participants. Estimated GFR values by the CG/BSA equation and the MDRD equation showed strong correlation (coefficient of correlation =0.85, $P < 0.001$) [Figure 1].

Prevalence of chronic kidney diseases

The K/DOQI guidelines were used for staging eGFR. Prevalence of reduced GFR (<60 mL/min/1.73 m²) by the CG/BSA equation was found to be 18.2% (95% confidence interval 14.6, 21.8). Prevalence of reduced GFR according to the MDRD equation was found to be 5.9% (95% confidence interval 3.7-8.1). Mean age of the study participants with reduced GFR (48±10 years) was significantly higher than that of the participants with normal GFR (>60 mL/min/1.73 m²) ($P < 0.001$). Table 1 shows the prevalence of various stages of GFR with respect to the age group of the study participants. Elderly women (>60 years) had the highest prevalence of reduced GFR (46.6%) compared with the other age groups.

Prevalence of chronic kidney diseases risk factors

Obesity and hyperlipidemia

BMI was calculated for 448 women, of which 108 (24.1%) were found to be obese. WC was measured in 453 women and 140 (30.9%) were categorized as obese (WC >80 cm). Mean cholesterol level was found to be 182.8±36.1 mg/dl. Hyperlipidemia (serum cholesterol >200 mg/dl) was reported in 132 (29.0%) participants.

Hypertension and diabetes mellitus

As per the JNC-7 classifications, 34 (7.4%) study participants were classified as hypertensive. Mean FBS level was found to be 85 gm/dl. Elevated FBS level (>126 gm/dl) was found in eight (1.8%) study participants.

Relationship of reduced glomerular filtration rate with chronic kidney diseases risk factors

On bivariate analysis, obesity (OR = 15.5), WC >80 cm (OR = 3.9), hyperlipidemia (OR = 2.5), age ($P < 0.001$), and calf circumference ($P < 0.001$) were found to be statistically significantly associated with reduced GFR. No statistically significant associations were observed between hypertension and DM with reduced GFR [Table 2].

In multivariate logistic regression analysis, all risk factors with P value < 0.1 were entered into the model. In the final model of regression, BMI ≥25 kg/m² (obesity) ($P = 0.002$), hyperlipidemia ($P = 0.017$), and age ($P < 0.001$) remained independent predictors of reduced GFR with

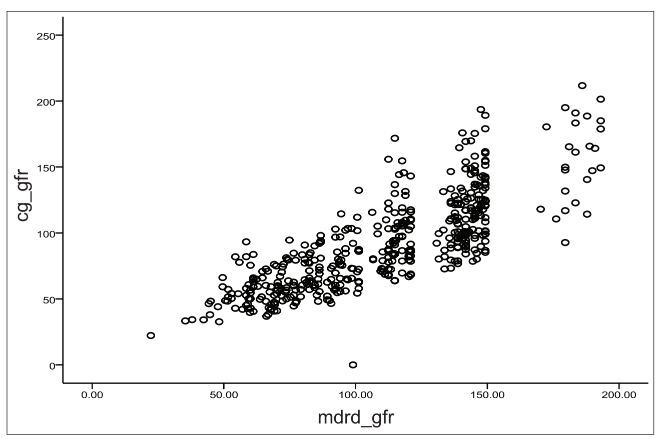

Figure 1: Correlation of estimated glomerular filtration rate (GFR) by the Cockcroft–Gault body surface area and modification of diet in renal disease equations. (CG-GFR: estimated GFR by Cockcroft–Gault equation, MDRD_GFR: modification of diet in renal disease (MDRD) equation)

Table 1: Prevalence of low glomerular filtration rate by the Cockcroft–Gault/Body surface area equation with respect to the age group of the study participants

GFR (mL/min/1.73 m^2)	Age group (years)			Prevalence (%)
	35-45	46-60	>60	
≥90	156	59	7	222 (48.8)
89-60	74	67	9	150 (33.0)
<60	42	27	14	83 (18.2)
Total	272	153	30	455

GFR: Glomerular filtration rate

Table 2: Relationship of reduced glomerular filtration rate with chronic kidney disease risk factors

CKD risk factor	Unadjusted OR (95% CI)	*P* value
Obesity	15.5 (3.7-64.2)	<0.001
WC >80 cm	3.9 (1.9-7.8)	<0.001
Hypertension	1.6 (0.5-4.9)	0.34
Diabetes mellitus	0.3 (0.08-1.5)	0.12
Hyperlipidemia	2.5 (1.3-4.7)	0.003
Age*	-	<0.001
Calf circumference*	-	<0.001

*Continuous variable: *t*-test applied, Bold: Statistically significant, OR: Odds ratio, CKD: Chronic kidney disease, CI: Confidence interval, GFR: Glomerular filtration rate, WC: Waist circumference

coefficient of regression (β) of –2.4, –0.85, and –0.06, respectively. Odd ratios for all other significant factors in the multivariate logistic regression analysis remained similar to the that in the bivariate analysis.

Discussion

CKD has been recognized as a risk factor for ESRD and CVDs, which are among the leading causes of death in developing countries. An interventional approach is necessary to prevent the development of CKD at a community level. This study was a cross-sectional, observational study conducted among perimenopausal women in selected villages of Haryana in north India.

This study reported a higher prevalence of reduced GFR by the CG/BSA and MDRD equations among women in the rural community. This study reported a higher prevalence of reduced GFR compared with the study by Singh, *et al*. (16.6%) among women in North India.[31] Two other community-based studies reported a much lesser prevalence of CKD at 0.79% and 1.39% by using serum creatinine cutoff of >1.8 mg% and MDRD equation, respectively.[23,24] The current study estimated the prevalence of CKD by using the CG/BSA and MDRD equations, as estimates on the basis of serum creatinine cutoffs are considered crude for epidemiologic studies, and it also underestimates the prevalence.[32,33] Estimation of GFR by the CG/BSA and MDRD equations has observed a good correlation ($r = 0.85$) consistent with the finding by Singh, *et al*.[31] The observed prevalence of CKD in this study is comparable with the findings of other community-based studies from other developed and developing countries.[33-39]

This study reported a higher prevalence of obesity (24.1%), central obesity (30.9%), and hyperlipidemia (29.0%) among women in the rural community. The prevalence of obesity was higher than that reported by the National Nutrition Monitoring Bureau (NNMB) data for adult women (10.9%) and NFHS-3 (2005-2006) report (1.3%) in the rural population.[40,41] Other studies from north India reported comparable results with this study.[31,42]

Age, BMI ≥25 (obesity), and hyperlipidemia levels were independent predictors of reduced GFR in this study. Various community-based studies in India also documented the association of reduced GFR with age, obesity, and hyperlipidemia.[23,24,31,43] Ikuo Nomura, *et al*. also documented the association of age, BMI and CKD in their study in the Japanese community.[44] Singh, *et al*. in their study reported the association of central obesity (WC >80 cm) with reduced GFR.[31] In the present study, WC >80 cm (central obesity) and calf circumference in women were found to be associated with reduced GFR in bivariate analysis, but lost its significance in multivariate analysis. Age might have acted as a confounding factor in the association of WC and calf circumference with reduced GFR.

This study reports a lower prevalence of hypertension (7.4%) and DM (1.8%) compared with previous studies.[31,42] The low prevalence of DM and hypertension might be attributed to high refusal (24.1%) to clinical examination and/or blood investigation in the study. In this study, the FBS level was used instead of the glucose tolerance test (GTT), which might have underestimated the prevalence of DM.[31] There was no association found between hypertension and diabetes with low GFR in contrast to various studies in the past.[45-47] This might be attributed to the small number of participants with diagnosed hypertension and DM.

The major limitation of the study was the high refusal rate (24.1%), which might have underestimated the results. Single blood estimation was the limiting factor in establishing chronicity of the kidney disease in the study population. It is known that the Indian population has a lower range of GFR compared with the population in developed countries, which is attributed to anthropometric phenotype, low protein intake, and possible genetic endowment with fewer nephrons.[26,31] This makes use of the CG and MDRD equations in GFR estimation questionable for the Indian population. Although CG and MDRD equations have been routinely used in hospital-based studies for the estimation of GFR, there is a lack of studies establishing the validity of these equations in the Indian population.[31,48] This study estimated GFR on the basis of these equations as it is one of the best possible ways to estimate GFR in community-based settings.

Conclusions

This study substantiates the fact that CKD is the rising public health problem in India, similar to that in the Western countries. It supports the fact that lifestyle-related diseases such as obesity and hyperlipidemia are also common in the rural community like in urban areas of the country. The association of modifiable risk factors with CKD gives an opportunity to prevent and control the rising burden of these disorders in the community. There is a need to develop a community-based intervention strategy encompassing screening for risk factors of CKD and increasing awareness about CKD in the community, particularly in high-risk groups such as perimenopausal women. Also, there is a need for more valid, ethnically appropriate, cost-effective measures or techniques for the estimation of GFR in the community-based setting for the Indian population.

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