



# Prevalence and predisposing factors of chronic kidney disease in Yazd city; a population-based study

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## ABSTRACT

**Introduction:** Chronic kidney disease (CKD) is a major health problem and one of the public health threats with an increasing prevalence and burden. However, early diagnosis of this disease is challenging in Iran due to insufficient information.

**Objectives:** In the present study, we aimed to determine the prevalence of CKD and its predisposing factors in Yazd city, Iran.

**Patients and Methods:** We conducted this cross-sectional study using the recruitment phase data of Yazd Health Study (YaHS) collected during 2013-2014. Data of 3649 individuals, age 20-69 years were analyzed. Glomerular filtration rate (GFR) was calculated using the modification of diet in renal disease (MDRD) formula and values less than 60 mL/min/1.73 m<sup>2</sup> were defined as CKD. Logistic regression was employed to determine the risk factors of CKD.

**Results:** The mean age of participants was 46.0 ± 13.8 years and the overall prevalence of CKD was 6.6 percent (7.6% for women and 5.4% for men). The disease prevalence was 21.5% in the age group of 60-69 years. The prevalence of CKD had a significant relationship with older age, obesity, female gender, diabetes, high blood pressure and history of heart disease.

**Conclusion:** CKD has a high prevalence in the population of this region of Iran. The most important modifiable risk factors for CKD included diabetes and high blood pressure. Therefore, the health system should strive for early detection of CKD in order to prevent morbidity and mortality of this disease.

### Implication for health policy/practice/research/medical education:

In a population-based study on 3649 participants in central of Iran, Yazd city, the overall prevalence of chronic kidney disease (CKD) was 6.6%. The most important modifiable risk factors for CKD included diabetes and high blood pressure. The health system should strive for early detection of CKD in order to prevent morbidity and mortality of CKD, especially in this region of Iran.

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## Introduction

Chronic kidney disease (CKD) is one of the public health challenges in the world (1) and its prevalence is increasingly high in developing countries (2). This disease ranked 27<sup>th</sup> among the causes of death in 1990, but by 2010, it ranked 18<sup>th</sup> (3). CKD is defined as a decrease in the amount of glomerular filtration or urinary excretion of albumin (4,5). The progression of the disease is usually mild and asymptomatic until the end-stage renal disease (ESRD).

At this stage, the function of kidneys decreases to less than 15 percent and the patient requires renal replacement treatments, such as dialysis or kidney transplantation to survive (6). The ESRD patients have a lower quality of life and life expectancy than the general population. In addition, reduction of the kidney function increases the risk of cardiovascular diseases and their related mortality rate (7). Although the CKD progresses over time, causes new problems and aggravates the previous complications,

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its progress may be reduced and its costly management may be avoided by early diagnosis.

Due to the late diagnosis of CKD in developing countries, most patients are identified at the late stages of the disease. The worldwide study over the burden of diseases showed that the mortality caused by CKD in Iran was less than one percent in 1990, but rose to higher than 2 percent in 2013. The reduction of GFR was also mentioned as one of the major causes of mortality in Iran (8). This increase in the prevalence of the disease requires urgent action and the first step is to measure the incidence and trends of CKD in Iran. Despite the extensive research in the developed countries, studies on the prevalence of CKD and its determinants are not enough in developing countries such as Iran (9). In previous studies conducted in Iran, fluctuations in the prevalence of CKD stages III-V in some provinces of Iran have been very different and wide and have been reported between 6 and 17% (10). This indicates the need to conduct this study in other parts of Iran. No studies have been conducted on the prevalence of the disease in central Iran, Yazd. Especially that diabetes, which is an important cause of CKD, has a high prevalence in this region of Iran (11). In addition, population-based studies were rarely conducted in Iran. The lack of basic and precise information on CKD in Iran prevented understanding the burden and early diagnosis of this disease. Therefore, high quality studies on CKD are required in Iran.

## Objectives

In this population-based study, we aimed to determine the prevalence of CKD and its determinants among the 20-69 years population using data from Yazd Health Study (YaHS) data (12).

## Patients and Methods

### Study design

This cross-sectional study was conducted on YaHS recruitment phase data collected during 2014-15 (12).

Ten thousand residents of Yazd Greater Area who aged 20-69 years old were selected using the cluster random sampling and took participate in YaHS. The YaHS researchers conducted interviews and calculated the anthropometric measurements (height, weight, waist circumference and hip circumference) and blood pressure according to a validated protocol. Details of YaHS have been published elsewhere (13). Overall, 40 percent of the participants (n=3825) agreed to give their blood samples for various tests to laboratory. Of them, 175 individuals were excluded because they did not have the required information for calculating GFR. Therefore, in the current study, we used the information collected from 3649 participants.

Demographic data including age, gender, educational level, marital status, and also history of tobacco smoking, cardiovascular diseases, diabetes and high blood pressure

were collected using a structured questionnaire. Physical examinations such as anthropometric measurements and blood pressure were conducted by trained staff. The abdominal circumference was measured to the nearest 0.1 cm with participants wearing light clothes and without any pressure on the body surface. The hip circumference was measured at the widest part of the buttocks using the same method. Then, the waist circumference was divided by the hip circumference and the waist-to-height ratio (WHR) was obtained. The risk levels were defined as  $WHR \geq 0.9$  cm in men and  $WHR \geq 0.85$  cm in women (13). A tape measure was employed to measure the height of participants in cm with no shoes, hat, or hair clip. The weight was also measured using Omron BF511 digital body scan (Omron Inc. Nagoya, Japan), with accuracy of 0.1 kg. The body mass index (BMI) was obtained by dividing the weight in kg by the height squared in meter. The BMI in the range of 25-29.9 kg/m<sup>2</sup> was defined as overweight and  $BMI \geq 30$  kg/m<sup>2</sup> showed obesity. Furthermore, we utilized the standard gauge pressure to measure the participants' blood pressure after five minutes of rest in sitting position. Blood pressure was measured three times from the right hand of the individual with at least five minutes interval; the mean of the last two measurements was calculated and defined as the participant's blood pressure. Hypertension was defined as systolic blood pressure of  $\geq 140$  mm Hg, diastolic blood pressure of  $\geq 90$  mm Hg or consumption of hypertensive blood pressure drugs (14).

After 12 hours of fasting, 10 mL of venous blood sample was collected from each participant. The biochemical tests including creatinine, fasting blood glucose, cholesterol, low-density lipoproteins (LDL-c), high-density lipoproteins (HDL-c) and triglycerides (TG) were measured using the enzyme colorimetric kits (Pars Azmon). In our analysis, low HDL-c was defined as less than 40 mL/dL in men and less than 50 mL/dL in women. Individuals with fasting blood sugar  $\geq 126$  mL/dL, history of diabetes or consumption of anti-diabetes medications were defined as patients with diabetes. Serum cholesterol  $\geq 200$  mL/dL, triglyceride  $\geq 150$  mL/dL and LDL-c  $\geq 130$  mL/dL were classified as higher than normal rates. The serum creatinine levels were measured according to the Jaffe's kinetic standard method (Pars Azmon). Furthermore, to calculate the estimated glomerular filtration rate (eGFR), the modification of diet in renal disease (MDRD) equation was used as recommended by the national kidney foundation (15,16). The eGFR formula is as follows:

$$GFR \text{ in mL/min/1.73 m}^2 = 175 \times SCr^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female})$$

The Kidney Disease Outcome Quality Initiative guidelines defined the CKD stage 1 as  $eGFR \geq 90$  mL/min/1.73 m<sup>2</sup> with evidence of kidney damage; stage 2, as eGFR in the range of 60-89 mL/min/1.73 m<sup>2</sup> (mild

decrease in GFR); stage 3, as eGFR in the range of 30-59 mL/min/1.73 m<sup>2</sup> (moderate decrease in GFR); stage 4, as eGFR in the range of 15-29 mL/min/1.73 m<sup>2</sup> (severe decrease in GFR); and stage 5, eGFR ≤ 15 mL/min/1.73 m<sup>2</sup> (dialysis-dependent; kidney failure). In this study, we considered the eGFR ≤ 60 mL/min/1.73m<sup>2</sup> as the CKD (stages 3 to 5).

### Data analysis

Moreover, all the continuous data with normal distribution were calculated as mean ± standard deviation and classified variables were indicated as percentages. The difference between the continuous variables was investigated using t-test and the differences among the classified variables were investigated by chi-square test. A multivariate logistic regression model was applied to evaluate the odds ratio (OR) of risk factors associated with CKD. All the statistical analyses were conducted using SPSS version 20 at the significance level of 0.05.

### Results

We studied a total of 3649 patients in the age range of 20-69 years with a mean age of 46.0 ± 13.8 years. Of the total population, 53.7% (n = 1960) were women. In terms of BMI, 39% of the participants were overweight and 30% were obese. Around 74.5% of the participants had abnormal WHR. In this study, the prevalence of type II diabetes and hypertension were 20.1% and 38.9%, respectively. Furthermore, 10.2% of patients had a history of smoking and 7.3% had a history of heart disease. The mean of eGFR was 84.1 ± 17.7 mL/min/1.73m<sup>2</sup> for the participants since women (82 mL/min/1.73 m<sup>2</sup>) had lower scores than men (86.0 mL/min/1.73 m<sup>2</sup>; *P* < 0.001).

The overall prevalence of CKD was 6.6% based on the eGFR calculated using the MDRD equation, (5.4% in men and 7.6% in women). The prevalence rates of CKD in individuals with and without diabetes were 14.3% and 4.7%, respectively. The CKD rates in participants with high blood pressure and normal blood pressure were 11.8% and 3.3%, respectively. Our findings showed that 95% of the CKD patients were in stage three, 3% were in stage four, and only 2% (n = 5) were in stage five. The prevalence of CKD increased with aging, thereby the prevalence of CKD among 50-59 year-old individuals was 21.5% (26% in women and 16.8% in men). In all the age groups, the incidence of CKD was higher in women than men (Table 1).

The mean age in CKD participants (59.8 ± 8.6 years) was significantly higher than the healthy individuals (45.6 ± 13.6 years; *P* < 0.001). The laboratory tests showed that the means of fasting blood sugar, serum creatinine, triglyceride, and serum cholesterol were significantly higher in CKD than non-CKD persons (*P* ≤ 0.05).

In the two-variable analysis, the factors associated with CKD were age, gender, diabetes mellitus, blood pressure, history of cardiovascular disease, BMI, WHR and serum HDL-c (Tables 2 and 3). In the multivariate analysis, we found a significant relationship between CKD and variables of age, gender, obesity, history of heart disease, diabetes and hypertension (Table 4). In the age group of 20-49 years, only high blood pressure was associated with CKD (*P* = 0.004).

We found that females had about 49% higher risk (OR = 1.49, 95% CI = 1.10–2.02) of having CKD than males. A trend of association was also observed between age and CKD. In other words, the odds of developing CKD for the age groups of 40-59 and 60-69 years were about 4.23 (95% CI = 1.90–9.44) and 25.04 (95% CI = 11.33–55.34), respectively, compared with the odds of 20-39 years age group. The risk of CKD was about 1.9 (95% CI = 1.3–2.8) times higher in obese persons compared with those with BMI < 25 kg/m<sup>2</sup>. The risk of CKD was about 1.46 (95% CI = 1.08–1.97) times higher in participants with diabetes in comparison with the non-diabetic individuals. The risk of CKD was about 1.53 (95% CI = 1.11–2.10) times higher in patients with hypertension than the non-hypertensive people. The risk of CKD was about 1.87 (95% CI = 1.28–2.72) times higher in patients with a history of CVD/ stroke compared with those with no history.

### Discussion

This study showed that the prevalence of CKD was 6.6 percent in people within the age range of 20-69 years in Yazd Greater Area; 5.4% in men and 7.6% in women. In addition, the prevalence of CKD among 50-59 year-old individuals was 21.5%. The city of Yazd is located in the central region of Iran. Compared to other provinces of Iran, it seems that the prevalence of this disease in Yazd has some differences and similarities with other regions of Iran

It has been reported that the prevalence of CKD is very different in studies conducted in Iran. The lowest prevalence of CKD is in Golestan province, which is 4.6% (17) and the highest prevalence in Urmia which is

**Table 1.** Prevalence of CKD among different age and gender groups of residents of Yazd Greater Area aged 20-69 years

Age group (y)	Men		Women		Total	
	N	CKD* (%)	N	CKD* (%)	N	CKD* (%)
20-39	531	3(0.6)	662	5 (0.7)	1193	8 (0.7)
40-59	764	23(3)	887	37 (4.2)	1651	60 (3.6)
60-69	394	66 (16.7)	411	107 (26)	805	173 (21.5)
Total	1689	92 (5.4)	1960	149 (7.6)	3649	241 (6.6)

**Table 2.** Comparison of potential risk factors between participants with and without CKD in residents of Yazd Greater Area aged 20-69 years

Characteristic		Total (N=3649)	CKD <sup>+</sup> (n=241)	CKD <sup>-</sup> (n=3408)	OR (95% CI)	P value
Age group (y)	20-39	1193	8	1185	1	
	40-59	1651	60	1591	5.59 (1.09-1.87)	<0.001*
	60-69	805	173	632	40.55 (19.83-82.91)	<0.001*
Gender	Male	1689	92	1597	1	
	Female	1960	149	1811	1.43 (1.09-1.87)	0.009*
BMI (kg/m <sup>2</sup> )	< 25	1081	38	1043	1	
	25-29.9	1358	93	1265	2.02 (1.37-2.97)	<0.001*
	≥ 30	1044	103	941	3.00 (2.05-4.40)	<0.001*
Waist to hip ratio	Normal	928	33	895	1	
	Abnormal	2706	208	2498	2.26 (1.55-3.29)	<0.001*
Present or past smoker	No	3176	201	2975	1	
	Yes	363	29	334	1.28 (0.86-1.93)	0.224
History of CVD/stroke	No	3384	191	3193	1	
	Yes	265	50	215	3.89 (2.77-5.46)	<0.001*
Diabetes mellitus	No	2915	136	2779	1	
	Yes	734	105	629	3.41 (2.61-4.46)	<0.001*
Hypertension	No	2231	73	2158	1	
	Yes	1418	168	1250	3.97 (2.30-5.27)	<0.001*

\* Significant at 95% confidence interval.

**Table 3.** Comparison of biochemical factors between participants with and without CKD in residents of Yazd Greater Area aged 20-69 years

Laboratory tests		CKD <sup>-</sup> (n=3408)	CKD <sup>+</sup> (n=241)	All (N=3649)	OR (95% CI)	P value
Low HDL-c	No	2331	134	2197	1	
	Yes	1318	107	1211	1.45 (1.11-1.89)	0.006*
LDL-c, mg/dL	<130	2538	159	2379	1	
	≥130	1098	81	1017	1.19 (0.90-1.57)	0.215
Cholesterol, mg/dL	<200	2111	124	1987	1	
	≥200	1536	115	1421	1.30 (1.00-1.68)	0.052
TG, mg/dL	<150	2089	105	1984	1	
	≥150	1558	134	1424	1.78 (1.36-2.32)	<0.001*

\* Significant at 95% confidence interval.

37.9% (18). Some of the probable causes of differences in these results are the difference in the method of measuring of serum creatinine, difference in the method of determining GFR, variations in the populations,

**Table 4.** Multiple logistic regression analysis of predictors of CKD

Characteristic		OR	95% CI	P value
Gender	Male	1	-	
	Female	1.49	1.10-2.02	<0.001*
Age groups	20-39	1		
	40-59	4.23	1.90-9.44	<0.001*
	60-69	25.04	11.33-55.34	<0.001*
BMI(kg/m <sup>2</sup> )	< 25	1		
	25-29.9	1.44	0.95-2.17	0.084
	≥ 30	1.70	1.12-2.60	0.014*
Diabetes mellitus	No	1		
	Yes	1.46	1.08-1.97	0.014*
Hypertension	No	1		
	Yes	1.53	1.11-2.10	0.009*
History of CVD/ stroke	No	1	-	
	Yes	1.87	1.28-2.72	0.001*

\* Significant at 95% confidence interval.

diversity in racial and ethnic and also age differences. In our study, the sampling method was population based on age more than 20 years and we utilized MDRD formula to measure kidney function. In addition, the definition of CKD was  $GFR \leq 60 \text{ mL/min/1.73 m}^2$ . Therefore, we decided to compare the results of our study with studies that, like ours, were population based and age and also used the MDRD method to determine GFR and the definition of CKD based on GFR was less than 60 mL/min/1.73 m<sup>2</sup>. These four characteristics mentioned in the research methodology were found in studies conducted in Golestan, Fars and Tehran provinces (10,17,19,20).

Khajehdehi et al calculated the prevalence of CKD in Fars province and indicated that the overall prevalence of the disease among people over 18 years of age was 11.6 percent (14.9% in women and 4.5% in men) and for those over 60 years was 31% (19). In the city of Gonabad, Naghibi et al reported that the prevalence of CKD in individuals aged 20-60 years was 5.1 percent (20). Najafi et al reported a prevalence of 4.6% for CKD based on GFR among adults ≥18 years in Golestan (17). Safari Nejad et al

carried out a comprehensive population-based study on 17 thousand of people over the age of 14 in Iran during 2002-2005 and reported that the prevalence of CKD was 7.8% (10). Moreover, in our study, the prevalence of CKD was 6.6 percent. Based on the above studies, which are based on general population and with a sample size of over one thousand and appropriate methodology in terms of CKD definition and also GFR calculation, the prevalence of CKD in Iran is between 4.6 and 11.6%. This difference can also be related to genetic differences, different prevalence of diabetes and hypertension, which are the important parameters of CKD.

In our study, the prevalence of CKD in older age groups was more than that of the younger age groups; the risk of the disease in age group of 69-60 years was approximately 25 times more than that of 20-39 years age group. Furthermore, Sepanlou et al estimated the prevalence of the disease in the age group of 40-75 years as 23.7% (26.6% in women and 20.6% in men) (9).

In a univariate analysis, most of the studied factors were correlated with CKD. However, in the multiple regression model, female gender, older ages, high blood pressure, diabetes and history of heart disease were the most important risk factors which were associated with CKD. In multivariate analysis, we observed that CKD did not have any significant relationship with WHR and serum lipids (triglyceride, HDL-c, LDL-c, and cholesterol).

In most studies, the chance of CKD was higher in women than men (21,22). We also found that the risk of CKD in women was 1.49 times higher than men. Most studies reported that diabetes and high blood pressure increased the chance of developing CKD (8,19,23). In this regard, we found that 43% of our population had diabetes and 70% had high blood pressure, which confirms the previous findings. The risk of CKD was higher in diabetic and hypertensive patients than in healthy individuals.

Previous studies detected, a significant relationship between the history of heart disease and CKD (9,22). In our study, this relationship was also significant and the risk of CKD in patients with heart disease was 1.87 times higher than the healthy participants.

As reported in most of the previous studies, BMI is one of the major risk factors of CKD (19,24). Obesity and high BMI can increase the risk of developing CKD (9). In our study, the risk of developing CKD was 1.7 times higher in obese ( $BMI > 30 \text{ kg/m}^2$ ) participants than the individuals with  $BMI \leq 25 \text{ kg/m}^2$ .

## Conclusion

CKD has a high prevalence in the population of this region of Iran. Considering the growing trend of aging and CKD risk factors such as diabetes and high blood pressure in Yazd, CKD will lead to significant health outcomes and expenditure of health resources. Furthermore, the health system should strive for early detection of CKD in order to

prevent morbidity and mortality of this disease.

## Limitations of the study

In our population-based study, we used an appropriate sample size. Moreover, standard methods of data collection and laboratory tests were applied. However, we were faced with several limitations; (a) we analyzed a cross-sectional data set, (b) we measured the serum creatinine only once; where ideally we could repeat the measurement three months later and (c) we did not collect the data related to urine albumin and protein excretion; therefore, the prevalence of CKD stage 1 and 2 could not be estimated in this population.

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## Authors' contribution

NN, MM and HM were the principal investigators of the study. NN, MM and HM were included in preparing the concept and design. NN and MM revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

## Conflicts of interest

The authors declare no competing interests.

## Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Research Council of Shahid Sadoughi University of Medical Sciences approved and funded YaHS with the code number of 70421 on 2 July 2014. This research project was also approved at the Ethics Committee of the University Research Council with the code number of 17/1/73941 on 8 July 2014. Additionally, ethical issues (including plagiarism, data fabrication, double publication) were completely observed by the authors.

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