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Estimation of the prevalence of chronic kidney disease: The results of a model based estimation in Kerman, Iran

Reza Tabrizi[1], Farzaneh Zolala[2], Maryam Nasirian[3], Mohammad Reza Baneshi[4]
Abbas Etminan[5], Eghbal Sekhavati[6], Mahmoud Khodadost[7], Ali Akbar Haghdoost*[8]

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Abstract

Background: Chronic kidney disease is asymptomatic until its last stages and though it is increasing globally, we are faced with paucity of a population-based model to assess this disease, particularly in developing countries. Therefore, the aim of this study was to estimate the prevalence and trends of CKD according to a new estimation method.

Methods: Using multiplier method, we estimated the numbers of different stages of CKD based on the number of patients with end stage renal failure from 2006 to 2016. The required multipliers were extracted from a simulation of the disease in Kerman following a dynamic model. The 95% uncertainty interval was computed using Monte-Carlo technique with 10,000 iterations.

Results: The prevalence of CKDA (GFR<=90mL/min/1.73m2) and CKDB (GFR less than 60mL/min/1.73m2) patients were estimated to be 7.6% (95% uncertainty interval (UI), 5.7-9.1%) and 1.1% (95% UI, 0.8-1.3%), respectively in 2011. The method revealed that the prevalence may rise up to 25.7% (95% UI, 18.2-32.5%) and 3.7% (95% UI, 2.7-4.5%) for CKDA and CKDB, respectively in 2016, indicating approximately 3.3 times increase for both figures.

Conclusion: This study predicted an increase in the prevalence of CKD in the future. This may be due to the increasing life expectancy of the population, the increase in the prevalence of non- communicable diseases such as hypertension and diabetes, or patients' survival due to receiving better support. Therefore, the policymakers should be concerned and well informed about this increase.

Keywords: Chronic Renal Failure, Chronic Kidney Disease, Multiplier Method, Prediction in Iran.

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Introduction

Chronic kidney disease (CKD) is a major health problem (1). The progress of CKD is usually smooth and without any significant symptoms until the last stage when the patient may only survive with either dialysis or kidney transplant (2-3).

National Health and Nutrition Evaluation Survey in the U.S. has demonstrated that the prevalence of CKD (except for ESRF) has risen from 10% in 1994-1998 to 13.1% in 199 9-2004 (4). Based on the annual report of United Network for Organ Sharing in 2002, among patients who enroll in daily waiting list, 16 would die and one would need kidney transplant every 15 minutes

[1]. MSc Student of Epidemiology, Health Policy Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. kmsrc89@gmail.com
[2]. Assistant Professor of Epidemiology, Regional knowledge Hub of HIV/AIDS Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. zolalafarzaneh@gmail.com
[3]. PhD Candidate of Epidemiology, Regional Knowledge Hub of HIV/AIDS Surveillance, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. maryamnasirian27@gmail.com
[4]. Associate Professor of Biostatistics, Research Centre for Modeling in Health, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. rbaneshi2@gmail.com
[5]. Assistant Professor of Nephrology Department, Department of Internal Medicine, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran. abbas_etminan@yahoo.com
[6]. Larestan School of Medical Sciences, Laretsan, Iran. sekhavati.papers@gmail.com
[7]. Department of Epidemiology, Faculty of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran. mahmodkhodadost@yahoo.com
[8]. (**Corresponding author**) MD, PHD of Epidemiology and Biostatistics, Research Center for Modelling in Health, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran. ahaghdoost@gmail.com

(5). More than 1.1 million ESRF patients have an annual increasing rate of 7% worldwide. It is predicted that more than 70% of the ESRF patients will be residents of the developing countries (6-7). Due to the aging of the societies and the high prevalence of predisposing chronic diseases such as diabetes mellitus and hypertension, the number of CKD cases has noticeably raised in the past years (8-9).

A few studies estimated the number of ESRF and CKD patients in Iran. According to the reports from the Management Center for Transplantation and Special Diseases (Ministry of Health), the number of registered ESRF patients was 24,000 and 40,000 in 2004 and 2009, respectively, which is a dramatic increase (10-11). In a study conducted in Iran, it was estimated that over 700, 000 people had CKD, and 61, 000 new cases of CKD would have been developed by 2004 (11-12). Different studies in Iran reported 6 to 17% prevalence for CKD (10). The discrepancy among these figures might be due to the differences in their methodologies, mainly sampling and renal failure verification techniques. Because CKD is usually asymptomatic, determining its prevalence using direct methods might be an underestimation (2). Therefore, using indirect methods and models may help to illustrate the level of the disease efficiently.

Different indirect methods, including the multiplier method, have been employed to estimate the prevalence of diseases (13). The multiplier method has been frequently used to estimate the size of hidden subpopulations such as female workers and injecting drug users (14). However, to the best of our knowledge, no study has estimated the prevalence of CKD using multiplier method in in Iran.

One of the advantages of this method is its ability to estimate the prevalence of the disease in different age groups, sexes and stages. Due to a paucity of population-based model to estimate CKD, the aim of this study was to implement a new and simple statistical model to estimate the prevalence and trends of CKD with accuracy.

Methods

Study Setting and Definition: This study used indirect methods based on the data gathered from Kerman, the largest province in southeast of Iran, with a population of around 620,000 and a dry climate.

In this study, CKD is defined as" abnormalities of kidney, structure or function, present for>3 months, with implications for health; and CKD is classified based on cause, glomerular filtration rate category, and albuminuria category (CGA)". Based on GFR category, there are five stages for CKD. These stages are determined according to the level of GFR and kidney damage. The total number of CKD was estimated for the two conditions: Stages one to five (GFR <=90 mL/min/1.73 m^2), and stages three to five (GFR less than 60 mL/min/1.73 m^2). We used the term CKD_A and CKD_B for these conditions, respectively (15-17).

Multiplier Method: The multiplier method was used to estimate the number of CKD cases among those aged over 20 in Kerman. Multiplier method is an indirect method that needs two parameters: Benchmark and multiplier. Benchmark parameter is defined as the number of persons who registered in the target centers (B_i) in a certain period of time,, so we used the total number of registered ESRF patients in Kerman as benchmark (B_i). In this context, multiplier parameters (m_i) are the ratio of the size of each stage of the disease to the size of its pervious stage; for example, m_1

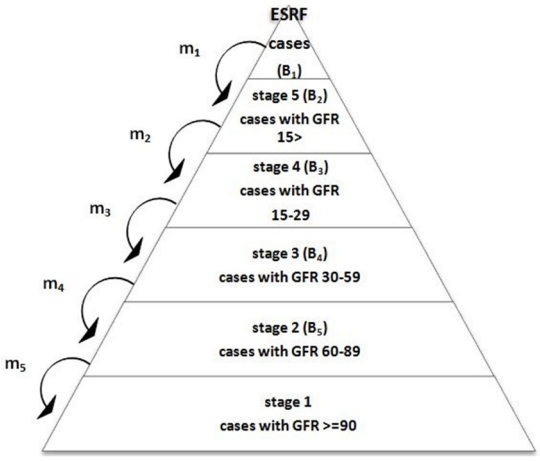

Fig. 1. Schematic of CKD (16) Estimation Method

is the size of ESRF over the size of patients in stage 5 (Fig. 1).

B_i parameter: The number of patients with hemodialysis and peritoneal dialysis or a kidney transplant was considered as the benchmark parameter in the first benchmark (B_1). Data were obtained based on census sampling method from all of dialysis and kidney transplant centers in Kerman. From 2006 to 2011, patients were classified by age group: 20-39, 40-59, <=60 years, and were counted. Then the number of patients was estimated in each stage and considered as a benchmark parameter for the next stage. For example, to estimate the number of people in stage 5, the number of ESRD patients who underwent renal replacement therapy (RRT) such as dialysis or kidney transplant was used as the benchmark parameter during the study (the proportion of ESRF patients of this study to the number of patients in stage 5). In this study, the number of patients in stage 5 was estimated using multiplier method. Moreover, this number (the number of patients estimated in stage 5) was considered as a benchmark parameter for estimating the number of patients in the previous stage (stage 4). In addition, the number of patients in stage 4 has been estimated considering the multiplier parameter of stage 4 (the proportion of stage 5 to stage 4). Moreover, the number of patients in all stages of CKD_A and CKD_B have been estimated with respect to the multiplier parameters and benchmark number in each stage.

m_i parameter: Due to the lack of access to multiplier parameters, a dynamic model was designed to simulate the parameters. The dynamic model requires reasonable inputs including age-specific annual incidence, death rate, and disease progression, which were estimated in each stage (18-20). Thus, a systematic review was conducted to obtain the above-mentioned inputs (Table 1). Unfortunately, no information was available on the inputs of age and stage of the disease in Iran; therefore, the literature of other countries was used. However, the validity of the finding about the input has been discussed during the group discussions with epidemiologists and interviews with experts. In addition, we tried to provide the lowest bias and highest accuracy for the impact of uncertainty in the inputs using statistical methods such as sensitivity analysis.

In this model, we assumed that the disease has started in the past and reached a stable trend over time. Moreover, we assumed that individuals were mixed in a random order, the population size was constant and the incidence, mortality and progression stages remained invariant over

Table 1. Inputs used in the Model to Simulate the Multiplier Parameters

Inputs	Value used (%)					Reference number
	$Stage_1$	$Stage_2$	$Stage_3$	$Stage_4$	$Stage_5$	
Age-group 20-39						
Rate* of ESRF in different stages of CKD	0.02	0.02	1.7	20.2	67.4	(19)
Rate** of disease progression in different stages of CKD	20	12	6	13	12	(20)
Rate** of death in different stages of CKD	7	12	21	35	15	(20)
Rate of death in ESRF under RRT			8.8			(21)
Age-group40-59						
Rate of ESRF in different stages of CKD	0.03	0.03	0.97	15.7	79.5	(19)
Rate of death in ESRF under RRT			16.2			(21)
Age-group>=60						
Rate of ESRF in different stages of CKD	0.03	0.03	0.37	7.2	4.6	(19)
Rate of death in ESRF under RRT			34.4			(21)
Output (multiplier parameter)	m_1	m_2	m_3	m_1	m_5	
Multiplier parameter in the age-group 20-39	86	18	46	6	863	
Multiplier parameter in the age-group 40-59	64	27	32	10	473	
Multiplier parameter in the age>=60	29	67	18	19	134	

*Annual Rate, **Due to the inaccessibility to the proper data, it was considered similar in all age groups.

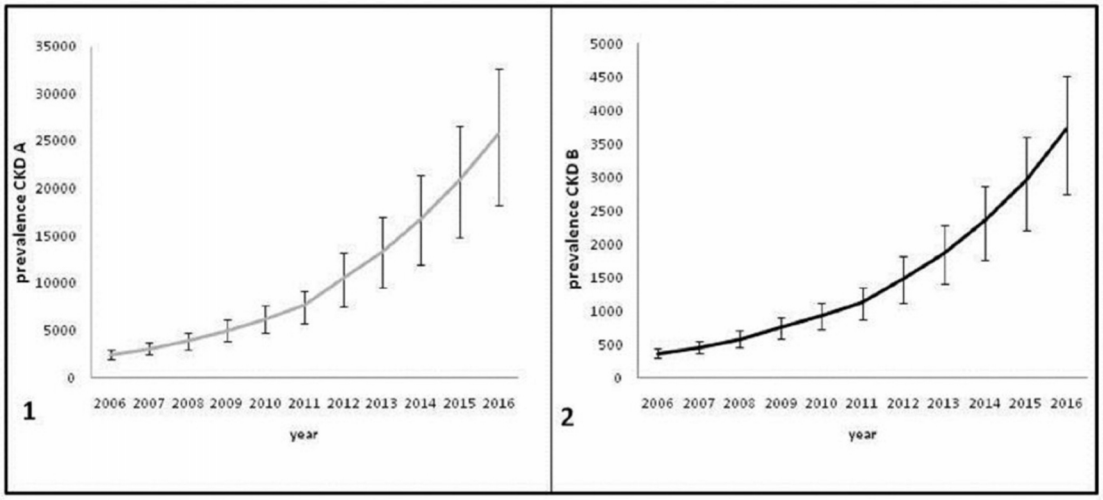

Fig. 2. The predicted prevalence of CKD_A (1) and CKD_B (2) per 100,000 population
* Graphs include 95% uncertainty interval

time. Based on the results of the dynamic model, a period of at least 20 years was required to reach a stable trend. Therefore, the dynamic model was developed based on the period from 1991 to 2011. The number of participants in each stage (1 to 5), and the multiplier parameters were subsequently calculated using "solver" commend in Excel (Table 1).

Sensitivity Analysis

Monte Carlo method was applied with 10,000 iterations in Stata Version 11 to provide 95% uncertainty interval (UI). We used normal distribution for all the parameters, which were derived from the dynamic model. The range between 2.5 and 97.5 percentiles was considered as 95% UI.

Results

Overall, from 2006 to 2011, 963 new Kermanian ESRF cases were registered (78 in 2006, 101 in 2007, 127 in 2008, 168 in 2009, 216 in 2010, and 273 in 2011). The annual growth rate was 28%; of which, around 15% were 20-39 year olds, 37% were 40-59, and 48% were over 60 years of age.

The Number and Prevalence Rate of CKD in a Population of Older than 20 Years of Age

The estimated number of CKD_A and CKD_B patients was 33,617 and 4,990, respectively in 2011 (Table 2 and Fig. 2). The estimated prevalence for this year was 7,668 for CKD_A and 1,138 for CKD_B. Our

Table 2. The Number and Prevalence of CKD_A and CKD_B Classified by Age Group and Year

		CKD_A			CKD_B		
Age Groups, Year		2006 (95% UI)	2011 (95% UI)	2016 (95% UI)	2006 (95% UI)	2011 (95% UI)	2016 (95% UI)
Number	20- 39	822 (549-1055)	2470 (1775-3171)	11231 (7055-15962)	103 (80-124)	307 (239-375)	1125 (828-1387)
	40- 59	2140 (1543-2728)	7580 (5443-9714)	31096 (20554-41554)	290 (220-359)	1031 (773-1284)	3900 (2789-4891)
	>=60	6143 (4216-8109)	21562 (15648-29607)	38936 (32256-42786)	974 (702-1243)	3769 (2550-4584)	11892 (8546-14586)
	All >=20	9100 (7059-11139)	33617 (25247-40032)	124315 (88280-157325)	1365 (1088-1643)	4990 (3857-5955)	17947(13308-21846)
Prevalence (per 100,000 population)	20- 39	354 (256-455)	958 (658-1175)	3943 (2477-5604)	44 (34-53)	114 (89-139)	359 (291-487)
	40- 59	2030 (1464-2588)	5979 (4222-7534)	20735 (13705-27708)	257 (209-341)	800 (600-996)	2601 (1860-3261)
	>=60	17390 (11935-22955)	53061 (39575-74879)	80550 (66730-88514)	2757 (1987-3519)	9038 (6449-11593)	24601 (17683-30175)
	All >=20	2442 (1894-2989)	7668 (5759-9131)	25731 (18272-32563)	366 (292-441)	1138 (880-1358)	3715 (2755-4522)

results revealed that the estimated prevalence was three times more in 2011 compared to 2006. Moreover, the predicted number of patients was 124,315 for CKD_A and 17,947 for CKD_B for 2016. The corresponding prevalence was 25,731 and 3,715 per 100,000 population aged over 20 (Fig. 2).

The Prevalence of CKD_A Classified by Age Group

In all age groups, the estimations for 2011 were about three times the estimations in 2006 (Fig. 3). The prevalence of CKD_A among 20-39 year-olds was 985 in 2011, which was 2.7 times more compared to 2006. The prevalence of the disease was 5,997 in 40-59 age group in 2011, which was 2.9 times more than that in 2006. The corresponding ratio for>=60 year-olds was 3.5. Our prediction indicate that in 2016 the prevalence of CKD_A will be 3,943, 20,735, and 80,550 for the 20-39, 40-59, and>=60 age groups, respectively (Fig. 3).

The Prevalence of CKD_B Classified by Age Group

Prevalence of CKD_B was 114 among the 20-39 year-olds in 2011, indicating a 2.5 times increase compared to 2006. A comparison of the prevalence of CKD_B among 40-59 year old individuals during these years shows a 3.1 time increase (257 vs. 800). The corresponding ratio for>=60 year-olds was 3.2 (Fig. 3 and Table 2). Our prediction shows that in 2016 the values will be nearly three times the values in 2011 in all age groups (Table 2).

Relationship between Age and CKD_A/ CKD_B Prevalence

Our results revealed that the prevalence of CKD_A and CKD_B increased with age (Table 2). In 2006, 2011, and 2016, the prevalence of CKD_A was at least five times higher in 40-59 year olds than those aged 20-39. Based on the estimated values for 2011 and 2006, the prevalence of the disease among those aged>=60 was around

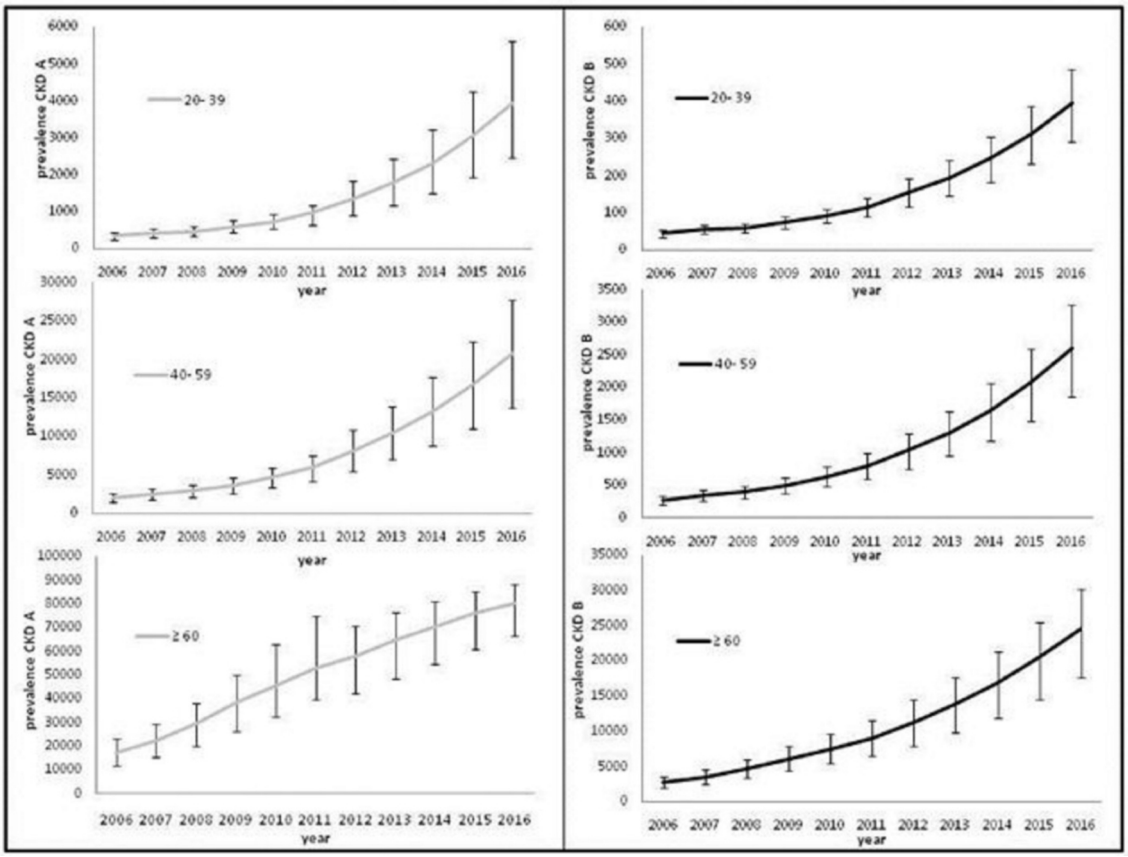

Fig. 3. The prevalence of CKD_A and CKD_B per 100,000 populations in different age groups, with 95% uncertainty interval

eight times higher than those aged 40-59. The corresponding figure for 2016 was four times as much (8,055 vs. 20,735). The prevalence of CKD_B among patients aged 40- 59 was about six times higher than 20-39 year-olds. Comparing>=60 to 40-59 year-olds, the corresponding figure was about ten times as much, which was more or less constant over time.

Discussion

The results of this study revealed that there would be an increase in the prevalence of CKD_A and CKD_B in Kerman and this is predicted to maintain in the future. In addition, we estimated a higher rate of the disease in older age groups. The prevalence of CKD_A and CKD_B was 7.6% and 1.1% in 2011, respectively. These prevalence figures are nearly three times more than those reported in 2006. These disorders are projected to increase in a rate of 3.3 in 2016 compared to the corresponding figures in 2011.

The prevalence of the disease was very different globally. The minimum and maximum reported CKD_A were 6.3% and 26.7% worldwide, while CKD_B was reported to be 1.3 % and 18.9 % (3, 21-22). Recent studies in Iran reported different prevalence for CKD_A and CKD_B. Hosseinpanah and colleagues reported a 18.9% prevalence for CKD_B in Iran (23). In a study conducted in Kalaleh (in northern Iran), the prevalence of CKD_B was reported to be 8.8% (10). In a study in Tehran, the capital of Iran, the prevalence of CKD_B was 6.5% among taxi drivers (6).

The differences between the prevalence estimated in the present study and other studies might be either due to the differences in the genetic factors, environmental effects, lifestyle, socioeconomic status of the society, and access to health care services. Furthermore, these differences could be due to the demographic pattern of the samples and different methodologies employed (10). Methodological differences are either in the serum creatinine measurement methods, the formula used to estimate GFR, or in the definition of albuminuria and proteinuria to diagnose CKD_A and CKD_B in different studies (24). For instance, in a study by Eynollahi and colleagues in Tehran, they measured the renal function in the first step, and estimated the prevalence of CKD_B to be 4.6%. However, when they rechecked the patients to confirm the disease, they found a 2% prevalence (25). The noticeable point is that the studies performed in Iran mainly used a single measurement to detect patients, and the MDRD formula is used without ethnic coefficient which could lead to the overestimation of the results.

However, a sharp time trend exists in the prevalence of this disease; therefore, the measured frequency of the disease might vary in different studies only due to a few year time intervals between the studies. In terms of the time trend of the disease, an increasing trend has been observed in most studies throughout the world, similar to our results. The increasing trend could be explained through the aging of the population and propagation of chronic diseases such as diabetes mellitus, hypertension, dyslipidemia, or it might be due to the higher existence of risk factors such as BMI imbalance, lack of physical activity, and ethnic and genetic factors (14,26). Because these factors are increasing, we may witness a higher rate of CKD_A and CKD_B in the future. However, a part of these growths might be due to the improvement of the diagnosis tests and the availability of heath care services such as dialysis centers, kidney transplant centers, and nephrologists (4).

A positive correlation was found between age and the prevalence of the disease. Most of the patients were older than 60 years, similar to other studies (27); for example CKD_A was eight times higher in>60 year-olds than in 40-59 year-olds, and CKD_B prevalence was 10 times higher in the>60 age groups than in 40-59 year-olds. Based on the prior studies across the world, we observed that the minimum and maximum prevalence of CKD_A was reported to be 1-

2.7% (27-28), 7.6-29.6% (10,28), and 23.4-38.3% (28-29) in 20-39, and 40-59 age groups and in population of over 60 years of age, respectively. Similarly for CKD_B, the minimum and maximum prevalence was 0.3-7% (30-31), 1.4-6.2% (31-32), and 8.14-23.59% (1,30), respectively. This could be explained through the reduction of renal function and the higher chance in occurrences of other risk factors associated with age increase (33-34) such as cardiovascular disease (CVD), diabetes, and hypertension.

Although this study was the first to apply an indirect method to estimate and predict the prevalence of CKD_A and CKD_B, it has some limitations. Like other prediction methods, the precision and validity of outputs depend on the model's assumptions. In addition, we might have missed some patients due to death before being admitted to dialysis and kidney transplant centers, and this could affect the benchmark parameter. However, changes in these numbers may not be significant because ESRF has obvious symptoms.

The policymakers in the National Health System in Iran should pay more attention to the early detection (screening) and management of these diseases. Moreover, this disease has an iceberg pattern. Thus, only a small proportion of patients with chronic kidney diseases have tangible and visible symptoms. As indicated in this study, many patients will reach higher stages of chronic kidney failure, and this supports our assumption that many people with ESRD will be unveiled.

We need a coherent plan to provide facilities, medical equipment (such as space, equipment, and beds for dialysis or transplantation) and the labor force necessary to respond to the patients' demands. In addition, the hidden and large part of the population will increase continually for reasons such as the increases of the general population's life expectancy, and the prevalence of chronic diseases like diabetes and high blood pressure. As a result, detection and diagnosis of these screening programs should be taken into account to delay or even prevent the progression of the disease to the end-stage renal failure.

Conclusion

This study was the first modeling study of CKD prevalence in Iran. The results of this study revealed that this disease might have a notable prevalence in the next few years, which would be more significant in older age groups. Therefore, there is an increasing need to develop services to provide appropriate care and treatment for the increased number of patients. Furthermore, annual or national screening of this disease should be implemented in the high-risk population, especially in the elderly.

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Conflict of Interest

None declared.

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