Chronic Kidney Disease in Isfahan Province, Action Plan for Screening in A Population-based Study

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Introduction. We intended to explore the prevalence of chronic kidney disease (CKD) and its different stages, as well as CKD associated variables in the adult population in Isfahan province, Iran.

Methods. Adults aged ≥ 18 were recruited in a cross-sectional study from 2017 to 2019. Data including demographics, anthropometrics, and laboratory findings were collected from each subject. The equation of chronic kidney disease- Epidemiology Collaboration (CKD-EPI) was used to estimate glomerular filtration rate (eGFR), and eGFR and UACR values were utilized to determine the stages of CKD.

Results. Data from a total of 3374 subjects was analyzed. The mean age of participants was 49.3 ± 14.09 years and 59.3% were female. The prevalence of CKD was 18.5%. Only 0.25 and 3.5% of the population were in CKD stage 3 and 4, while most of the patients were in CKD stage 2 (7.6%) and stage 1 (7.1%). CKD patients were mostly on refined grains diet and used lesser dairy products compared to healthy participants. Variables including systolic blood pressure (OR = 1.018; $P < .001$), diastolic blood pressure (OR = 1.005; $P < .05$), fasting blood sugar (OR = 1.011; $P < .001$), female sex (OR = 1.319; $P < .05$), body mass index (OR = 1.030; $P < .05$), married status (OR = 1.335; $P < .05$), and smoking (OR = 1.529; $P < .05$) were significantly associated with increased risk of CKD in the logistic regression analysis.

Conclusion. According to our results, the prevalence of CKD, especially stages 1 and 2, is quite high in central part of Iran. These findings help us to improve the screening for CKD patients and perform larger scale studies to identify the challenges ahead.

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Original Paper

INTRODUCTION

Comprehensive data indicate that chronic kidney disease (CKD) is becoming progressively prevalent and the burden of the disease is quite high.[1] A meta-analysis of prevalence studies in 44 countries reported a 13.4% prevalence of CKD

worldwide.[2] Global evidence also show that 10.4% of men and 11.8% of women are involved with this condition.[3] Increased risk of acute kidney injury, end-stage kidney disease (ESKD), cardiovascular disorders (CVDs), mineral and bone disease, infections, impaired cognitive function, and, higher risk of mortality are some of the major known consequences of CKD.[4] Therefore, measures to control CKD progression and population-based preventive programs are imperative.

Various studies are available regarding the prevalence of CKD, but they are mostly from the United States and Europe. In addition Asian countries including Singapore, China, and Japan, have reported a prevalence of 6.6, 4.2, and 28.8%, respectively.[5-7] However, robust knowledge of CKD epidemiology in most low- and middle-income countries (LMICs) is still lacking.[5] Accordingly, epidemiologic studies in LMICs located in the Middle East region revealed limited data, even though the burden of the disease is assumed to be higher than expected.[6] Considering the burden of CKD in LMICs, a better perception of CKD epidemiology in these countries including those in the less-developed areas of the Middle-East region is urgently required.

The prevalence of CKD seems to be increasing in Iran, which could be mostly attributed to the aging of the population and increased prevalence of hypertension and diabetes.[7] Studies performed in Iran are limited to a number of provinces, and the prevalence of CKD in most areas is still unknown.[8-11] The prevalence of CKD is highly heterogeneous in different populations and is yet to be determined in many regions of Iran. This helps to encourage healthcare systems and facilities for programing of early detection and management of the disease. Isfahan, a large province located in the center of Iran, also lacks enough data regarding CKD prevalence. The authors of this paper decided to determine the prevalence of CKD and its risk factors in Isfahan province population.

MATERIALS AND METHODS

Study Design And Participants

This cross-sectional population-based study was conducted in cooperation with Isfahan University of Medical Sciences. Participants were selected from subjects who visited the health care centers within Isfahan city for regular check-up and screening. The eligibility criteria included adults 18 years and above, living in Isfahan, willing to participate in the study, without any symptoms of fever and common cold at the time of performing laboratory tests, and not engaged in heavy exercise during the past 48 hours of doing laboratory tests. Those with incomplete questionnaires or not willing to do the tests accurately were excluded. Pregnant women or those in the menstruation period were also excluded from the study. Figure 1 shows the overall scheme of the study (Figure 1).

Laboratory Tests

CKD was defined as eGFR of less than 60 mL/ min/ 1.73 m2 or markers of kidney damage such as albuminuria (presence of albumin equivalent to or greater than 30 mg/gr creatinine in a first morning urine sample) and hematuria (RBC count $\geq$ 2 per high power field in the urine analysis).[12,13]

All parameters were measured in the same laboratory. Blood samples were collected after an overnight fast for at least 12 hours. Urine albumin and creatinine levels were measured using a first morning urine sample. Urine dipsticks (MN Analytic-One kit, Qatar) were used for urine analysis. Serum and urine creatinine levels were measured using the Jaffè calorimetric method on a Hitachi-917 auto-analyzer (Pars Azmun kit, Iran). The urine albumin level was measured using the calorimetric method on a Hitachi-917 auto-analyzer (Randox, England). Then urine albumin to creatinine ratio (ACR) was calculated by dividing the urine albumin by urine creatinine and expressed as milligrams per gram of creatinine. Subjects with ACR of less than 30, 30-299, and equal or higher than 300 mg/gr, were classified as normal (A1), moderately increased albuminuria (A2), and severely increased albuminuria (A3), respectively. All cases with ACR > 30 mg/g were tested again during the next 3 to 6 months. Estimated GFR (eGFR) was calculated by Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation using a calculator.[14] The Kidney Disease: Improving Global Outcomes (KDIGO) guideline was used to define CKD stages.[12]

Other laboratory parameters including fasting blood glucose and serum triglyceride (GOD-PAP method), serum levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol (CHOD method) were measured by enzymatic colorimetric

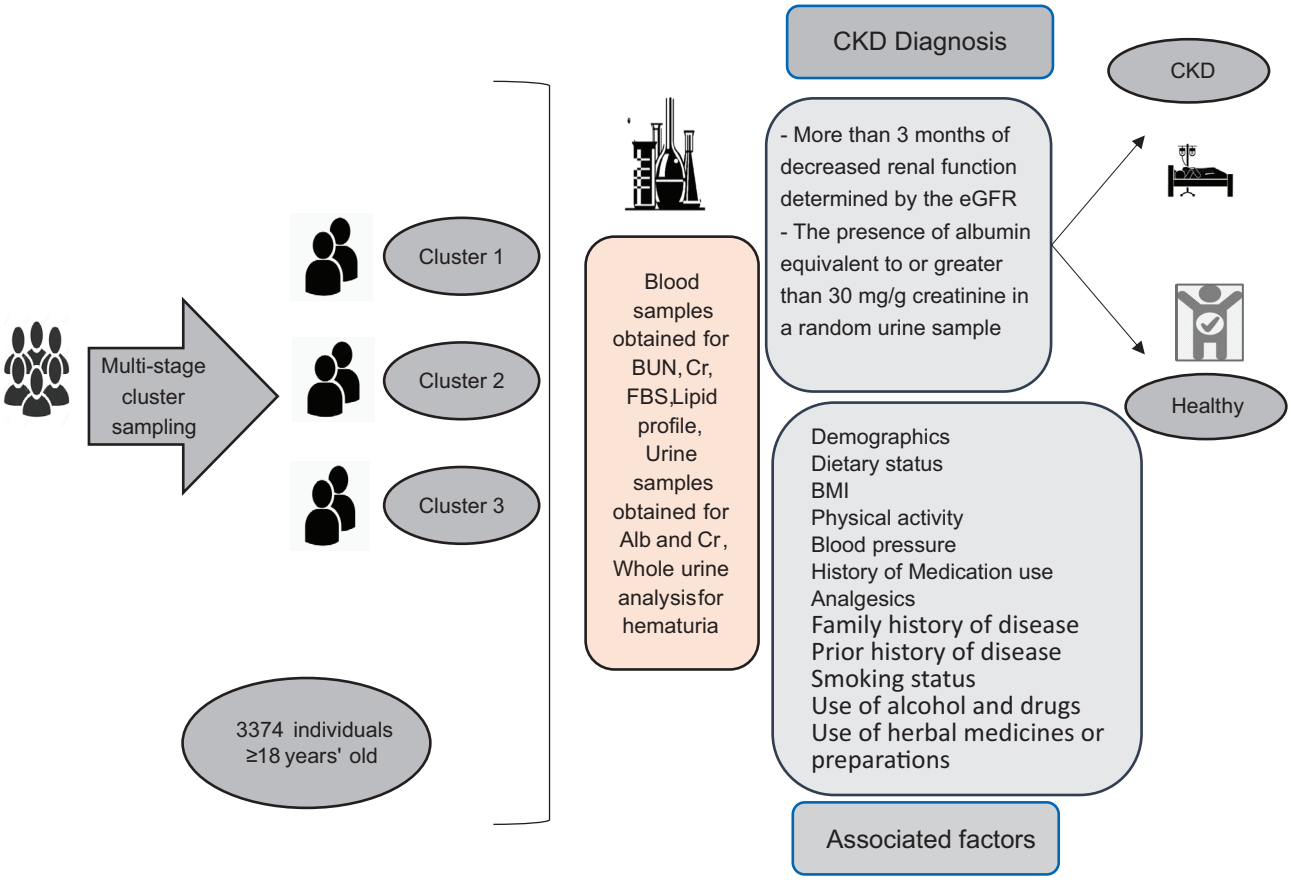

Figure 1. The Scheme of this study

method using Pars-Azmun kits on a Hitachi-917 auto-analyzer. Blood Urea Nitrogen (BUN) was also measured using the Urease GLDH method on a Hitachi-917 analyzer (Adit kit).

Other Assessments

Systolic and diastolic blood pressures (SBPs and DBPs) were measured by the same digital sphygmomanometer (Omron BF511 (Omron Corp, Kyoto, Japan)) from the right arm in all patients. If the first BP reading was equal to or above 140/90 mmHg, a second measurement was carried out 15 min after the first measurement, and the mean of the first and second measurements was recorded. All participants were weighed with a single mechanical scale (Zyklusmed ZYK-MS01, China) with 0.01 kg accuracy with minimal clothing and no shoes. We also used a non-stretched measuring tape for height measurement without shoes, to the nearest 1 mm, (Seca, USA). Body Mass Index (BMI) was calculated with the help of "weight (kg) to height, to the power of 2, (m^2)" equation. A semi-quantitative food frequency questionnaire (FFQ)[15], including 117 items, designed based on Willet format, was applied for dietary assessment including standard serving size for each item. To assess each individual's habitual physical activities during the past year, the Baecke questionnaire was used.[16] This questionnaire consists of three main domains of individual physical activities (sport, occupational, recreational) with 16 questions.

Additional demographic parameters, including gender, age, marital status, level of education, residence area, smoking, opium and substance abuse, alcohol use, use of medications (acetaminophen or non-steroidal anti-inflammatory drugs (NSAID) such as ibuprofen, diclofenac, celecoxib, indomethacin, ketorolac tablets/capsules, suppositories, or injections) more than once a day for more than two weeks, self-reported history of cardiovascular diseases, diabetes, and hyperlipidemia, positive family history of cardiovascular disease, diabetes,

hypertension, hyperlipidemia and kidney disease in first-degree relatives, and use of herbal medicines or preparations were assessed by an electronic questionnaire (www.ckd-epidemiology.ir).

Statistical Analysis

Descriptive data were presented as mean ± SD for quantitative and number (percent) for qualitative variables. The overall prevalence of CKD and its prevalence in relation to age, gender, and other exposure variables were estimated. The contribution of various variables based on subjects' characteristics in two groups (healthy and diagnosed with CKD) was assessed by univariate comparisons and multivariate modeling. In the univariate analysis of recorded factors, comparisons were conducted using independent paired t-test or Mann-Whitney tests. In order to compare qualitative variables in two groups, a Chi-squared test was applied. Multivariate logistic regression was used to determine the contribution of various exposure variables in CKD prevalence. Prevalence in Isfahan was then compared with similar populations using the Binominal test. SPSS software, version 20 (SPSS Inc., Chicago, IL, USA) was used for all statistical analysis. *P* value < .05 was considered significant.

RESULTS

In total, 3374 individuals with complete information were included in the current study. The overall prevalence rate of CKD was 18.5% among population visiting health care centers in Isfahan province (Figure 2). As is shown in Table 1, most of the CKD and non-CKD patients were between 45 to 64 years old with a mean age of 49.3 years. Our study population mostly consisted of females (59.3%). Females were predominantly in stages of 1-A1 to 3a-A1 while the number of male subjects was relatively more in higher stages. Most of the study population were married (85.5%) and had elementary education (36.3%). In addition, they were mostly non-smoker (84.1%), and without any history of opioid (96.8%) or alcohol (96.3%) use (Table 1).

The laboratory parameters, anthropometric data, and physical activity of the study population are presented in Table 2. Patients with CKD tended to have higher BMI and SBP, as well as lower LDL and HDL cholesterol, and physical activity compared to the non-CKD subjects. Those in the CKD stage 4-A3 had the highest BMI and SBP and lowest physical activity, as well as the highest LDL and the lowest HDL levels.

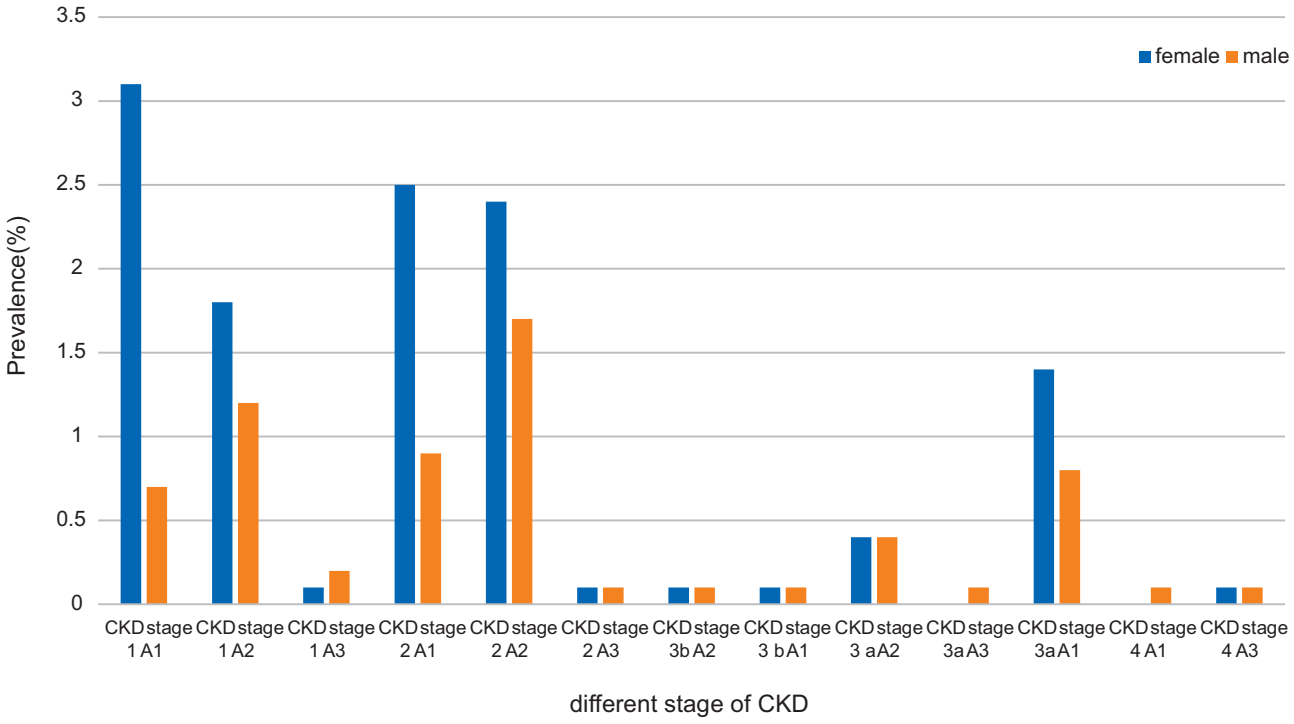

Figure 2. Distribution of CKD different stages prevalence based on the Gender

Table 1. Descriptive Statistics for Qualitative Variables Based on CKD Stage Groups

Variables	CKD Stage 1A1	CKD Stage 1A2	CKD Stage 1A3	CKD Stage 2A1	CKD Stage 2A2	CKD Stage 2A3	CKD Stage 3bA2	CKD Stage 3bA1	CKD Stage 3aA2	CKD Stage 3aA3	CKD Stage 3aA1	CKD Stage 4A1	CKD Stage 4A3	CKD (sum)	Not CKD	Total	*P*
Age, y (n (%))																	
18 to 44	88 (2.6)	54 (1.6)	3 (0.1)	34 (1.0)	13 (0.4)	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	196 (5.8)	1140 (33.8)	1336 (39.6)	
45 to 64	35 (1.0)	46 (1.4)	7 (0.2)	59 (1.7)	63 (1.9)	5 (0.1)	1 (0.0)	1 (0.0)	7 (0.2)	1 (0.0)	29 (0.9)	1 (0.0)	4 (0.1)	259 (7.7)	1261 (37.4)	1520 (45.1)	< .01
65 to 74	5 (0.1)	3 (0.1)	0 (0.0)	14 (0.4)	45 (1.3)	1 (0.0)	4 (0.1)	2 (0.1)	11 (0.3)	1 (0.0)	28 (0.8)	0 (0.0)	3 (0.1)	113 (3.5)	278 (8.1)	391 (11.6)	
> 75	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.2)	17 (0.5)	1 (0.0)	3 (0.1)	5 (0.1)	7 (0.2)	0 (0.0)	17 (0.5)	1 (0.0)	0 (0.0)	58 (1.8)	69 (2.0)	127 (3.8)	
Gender (n (%))																	
Female	103 (3.1)	61 (1.8)	3 (0.1)	83 (2.5)	81 (2.4)	5 (0.1)	4 (0.1)	3 (0.1)	13 (0.4)	0 (0.0)	48 (1.4)	0 (0.0)	3 (0.1)	407 (12.1)	1593 (47.2)	2000 (59.3)	< .001
Male	25 (0.7)	42 (1.2)	7 (0.2)	31 (0.9)	57 (1.7)	2 (0.1)	5 (0.1)	5 (0.1)	13 (0.4)	2 (0.1)	28 (0.8)	2 (0.1)	4 (0.1)	223 (6.6)	1151 (34.1)	1374 (40.7)	
Marital Status (n (%))																	
Married	112 (3.3)	87 (2.6)	8 (0.2)	96 (2.8)	109 (3.2)	7 (0.2)	7 (0.2)	7 (0.2)	16 (0.5)	2 (0.1)	59 (1.7)	2 (0.1)	7 (0.2)	519 (15.4)	2365 (70.1)	2884 (85.5)	< .05
Single	16 (0.5)	16 (0.5)	2 (0.1)	18 (0.5)	29 (0.9)	0 (0.0)	2 (0.1)	1 (0.0)	10 (0.3)	0 (0.0)	17 (0.5)	0 (0.0)	0 (0.0)	111 (3.4)	379 (11.2)	490 (14.5)	
Education (n (%))																	
College Education	33 (1.1)	28 (0.8)	0 (0.0)	17 (0.5)	5 (0.1)	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	7 (0.2)	1 (0.0)	0 (0.0)	92 (2.7)	556 (16.5)	648 (19.2)	
Illiterate	6 (0.2)	8 (0.2)	2 (0.1)	25 (0.7)	41 (1.2)	2 (0.1)	5 (0.1)	1 (0.0)	10 (0.3)	1 (0.0)	29 (0.9)	0 (0.0)	2 (0.1)	132 (3.9)	318 (9.4)	450 (13.3)	< .001
School Education	89 (2.7)	67 (2.0)	8 (0.2)	72 (2.2)	92 (2.8)	5 (0.1)	3 (0.1)	7 (0.2)	16 (0.5)	1 (0.0)	40 (1.2)	1 (0.0)	5 (0.1)	406 (12.1)	1870 (55.4)	2276 (67.5)	
Smoking																	
No	121 (3.6)	83 (2.5)	8 (0.2)	101 (3.0)	115 (3.4)	7 (0.2)	8 (0.2)	8 (0.2)	25 (0.7)	2 (0.1)	72 (2.1)	1 (0.0)	5 (0.1)	556 (16.5)	2280 (67.6)	2836 (84.1)	< .05
Yes	7 (0.2)	20 (0.6)	2 (0.1)	13 (0.4)	23 (0.7)	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	4 (0.1)	1 (0.0)	2 (0.1)	74 (2.1)	464 (13.8)	538 (15.9)	
Alcohol Use																	
No	124 (3.7)	100 (3.0)	9 (0.3)	113 (3.3)	133 (3.9)	7 (0.2)	9 (0.3)	8 (0.2)	25 (0.7)	2 (0.1)	75 (2.2)	1 (0.0)	7 (0.2)	613 (18.2)	2636 (78.1)	3249 (96.3)	> .05
Yes	4 (0.1)	3 (0.1)	1 (0.0)	1 (0.0)	5 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	0 (0.0)	17 (0.5)	108 (3.2)	125 (3.7)	
Opioid Use																	
No	123 (3.6)	103 (3.1)	10 (0.3)	113 (3.3)	135 (4.0)	7 (0.2)	9 (0.3)	8 (0.2)	25 (0.7)	2 (0.1)	75 (2.2)	1 (0.0)	6 (0.2)	617 (18.3)	2649 (78.5)	3266 (96.8)	<.05
Yes	5 (0.1)	0 (0.0)	0 (0.0)	1 (0.0)	3 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	1 (0.0)	1 (0.0)	13 (0.4)	95 (2.8)	108 (3.2)	

P value is reported for comparison between CKD-stage.

Table 2. Descriptive Statistics for Quantitative Variables Based on CKD Stage Groups

Variables	CKD Stage 1A1	CKD Stage 1A2	CKD Stage 1A3	CKD Stage 2A1	CKD Stage 2A2	CKD Stage 2A3	CKD Stage 3bA2	CKD Stage 3bA1	Total	*P*
Triglyceride, mg/dL	135.91 ± 63.99	150.29 ± 64.66	258.10 ± 123.49	155.52 ± 68.17	165.04 ± 67.25	155.57 ± 39.59	144.11 ± 72.91	147.12 ± 34.13	154.32 ± 68.94	<.001
Total Cholesterol, mg/dL	161.88 ± 42.17	173.65 ± 52.23	180.90 ± 19.23	176.68 ± 52.27	175.96 ± 51.26	187.57 ± 51.88	143.33 ± 17.27	153.75 ± 31.32	171.47 ± 49.73	>.05
HDL, mg/dL	51.54 ± 10.89	50.55 ± 10.30	41.60 ± 5.98	51.55 ± 11.04	49.47 ± 10.67	55.57 ± 4.75	41.78 ± 5.16	42.88 ± 5.19	50.99 ± 11.07	<.05
LDL, mg/dL	90.90 ± 24.03	88.85 ± 30.23	99.90 ± 19.83	101.40 ± 36.35	97.83 ± 32.09	79.0 ± 29.32	72.78 ± 16.82	82.50 ± 26.79	96.51 ± 30.53	<.05
FBS, mg/dL	82.87 ± 9.60	94.14 ± 36.46	104.30 ± 60.20	88.41 ± 16.75	105.21 ± 46.73	148.14 ± 113.46	136 ± 86.78	94.38 ± 17.84	88.50 ± 24.01	<.001
SBP, mmHg	113.09 ± 19.59	121.88 ± 17.20	140.30 ± 26.73	123.32 ± 18.13	135.77 ± 22.41	142.14 ± 27.79	148.89 ± 19.12	147.63 ± 23.94	121.33 ± 19.43	<.001
DBP, mmHg	62.92 ± 28.31	70.65 ± 27.55	88.60 ± 21.57	68.71 ± 27.24	71.30 ± 31.04	65.71 ± 41.31	73.44 ± 26.01	83.38 ± 23.10	66.63 ± 28.41	<.05
BMI, kg/m^2	26.08 ± 4.37	27.39 ± 5.86	30.41 ± 6.78	27.08 ± 4.75	28.22 ± 4.53	29.18 ± 4.89	29.53 ± 5.79	27.72 ± 2.28	26.81 ± 4.79	<.001
Waist to Hip Ratio	0.893 ± 0.20	0.899 ± 0.091	0.894 ± 0.25	0.895 ± 0.083	0.957 ± 0.10	0.930 ± 0.11	0.958 ± 0.10	0.899 ± 0.32	0.921 ± 1.18	>.05
Physical Activity Index	6.85 ± 1.29	7.06 ± 1.54	7.54 ± 1.29	6.51 ± 1.23	6.50 ± 1.33	6.50 ± 1.95	6.45 ± 1.59	7.01 ± 1.53	6.86 ± 1.33	<.05
Variables	**CKD Stage 3aA2**	**CKD Stage 3aA3**	**CKD Stage 3aA1**	**CKD Stage 4A1**	**CKD Stage 4A3**	**CKD (sum)**	**Not CKD**		**Total**	***P***
Triglyceride, mg/dL	162.31 ± 29.34	160.0 ± 52.32	165.17 ± 75.45	128.00 ± 54.22	175.43 ± 46.39	155.73 ± 69.13	154.00 ± 68.90		154.32 ± 68.94	<.001
Total Cholesterol, mg/dL	169.69 ± 45.42	138.50 ± 48.79	174.21 ± 44.78	191.50 ± 48.79	168.43 ± 42.50	171.68 ± 48.64	171.43 ± 49.98		171.47 ± 49.73	>.05
HDL, mg/dL	48.85 ± 10.80	41.0 ± 5.65	48.16 ± 8.29	43.50 ± 10.60	46.0 ± 9.22	49.93 ± 10.40	51.24 ± 11.20		50.99 ± 11.07	<.05
LDL, mg/dL	91.77 ± 33.52	121.0 ± 25.45	93.45 ± 36.54	83.0 ± 26.87	75.86 ± 28.16	93.87 ± 31.66	97.12 ± 30.24		96.51 ± 30.53	<.05
FBS, mg/dL	97.48 ± 25.63	112 ± 26.87	99.89 ± 32.26	97 ± 19.79	95.29 ± 31.35	95.31 ± 35.86	86.95 ± 20.04		88.50 ± 24.01	<.001
SBP, mmHg	137.92 ± 25.54	129.0 ± 1.41	132.34 ± 19.06	120.0 ± 0.00	162.71 ± 16.58	127.04 ± 22.31	120.02 ± 18.46		121.33 ± 19.43	<.001
DBP, mmHg	70.28 ± 27.81	74.0 ± 2.82	71.47 ± 26.24	79.00 ± 9.89	85.43 ± 35.85	69.59 ± 28.51	65.95 ± 28.35		66.63 ± 28.41	<.05
BMI, kg/m^2	27.41 ± 5.55	25.15 ± 1.31	27.37 ± 5.35	29.27 ± 3.76	30.90 ± 3.74	27.39 ± 5.01	26.68 ± 4.74		26.81 ± 4.79	<.001
Waist to Hip Ratio	0.929 ± 0.22	0.979 ± 0.00	0.921 ± 0.08	0.956 ± 0.02	0.972 ± 0.056	0.916 ± 0.13	0.922 ± 1.31		0.921 ± 1.18	>.05
Physical Activity Index	6.97 ± 1.50	6.56 ± 0.088	6.56 ± 1.55	7.18 ± 1.14	6.35 ± 1.05	6.71 ± 1.40	6.90 ± 1.31		6.86 ± 1.33	<.05

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high density lipoprotein; LDL, low density lipoprotein; SBP, systolic blood pressure.
P value is reported for comparison between CKD-stage.

Table 3. Descriptive Statistics for Drug Usage Based on CKD Stage Groups

Drug Usage	CKD Stage 1A1	CKD Stage 1A2	CKD Stage 1A3	CKD Stage 2A1	CKD Stage 2A2	CKD Stage 2A3	CKD Stage 3bA2	CKD Stage 3bA1	CKD Stage 3aA2	CKD Stage 3aA3	CKD Stage 3aA1	CKD Stage 4A1	CKD Stage 4A3	CKD (sum)	Not CKD	Total	*P*
NSAIDs																	
No	88 (2.6)	77 (2.3)	7 (0.2)	84 (2.5)	96 (2.8)	6 (0.2)	7 (0.2)	6 (0.2)	22 (0.7)	2 (0.1)	60 (1.8)	1 (0.0)	7 (0.2)	463 (13.7)	1989 (59.0)	2452 (72.7)	> .05
Yes	40 (1.2)	26 (0.8)	3 (0.1)	30 (0.9)	42 (12)	1 (0.0)	2 (0.1)	2 (0.1)	4 (0.1)	0 (0.0)	16 (0.5)	1 (0.0)	0 (0.0)	167 (4.9)	755 (22.4)	922 (27.3)	
Acetaminophen																	
No	122 (3.6)	98 (2.9)	10 (0.3)	109 (3.2)	127 (3.8)	7 (0.2)	9 (0.3)	8 (0.2)	24 (0.7)	2 (0.1)	74 (2.2)	2 (0.1)	7 (0.2)	599 (17.7)	2638 (78.2)	3237 (95.9)	> .05
Yes	6 (0.2)	5 (0.1)	0 (0.0)	5 (0.1)	11 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	31 (1.0)	106 (3.1)	137 (4.1)	
ACEIs																	
No	128 (3.8)	103 (3.1)	10 (0.3)	114 (3.4)	135 (4.0)	6 (0.2)	8 (0.2)	8 (0.2)	25 (0.7)	2 (0.1)	74 (2.2)	2 (0.1)	7 (0.2)	622 (18.4)	2726 (80.8)	3348 (99.2)	< .001
Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.1)	1 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	8 (0.3)	18 (0.5)	26 (0.8)	
ARBs																	
No	121 (3.6)	91 (2.7)	7 (0.2)	95 (2.8)	96 (2.8)	7 (0.2)	2 (0.1)	3 (0.1)	15 (0.4)	0 (0.0)	46 (1.4)	2 (0.1)	2 (0.1)	485 (14.4)	2400 (71.1)	2885 (85.5)	< .001
Yes	7 (0.2)	12 (0.4)	3 (0.1)	19 (0.6)	42 (1.2)	2 (0.1)	7 (0.2)	7 (0.2)	11 (0.3)	2 (0.1)	30 (0.9)	0 (0.0)	7 (0.2)	145 (4.3)	344 (10.2)	489 (14.5)	
CCBs																	
No	128 (3.8)	102 (3.0)	10 (0.3)	113 (3.3)	135 (4.0)	7 (0.2)	9 (0.3)	6 (0.2)	26 (0.8)	2 (0.1)	74 (2.2)	2 (0.1)	7 (0.2)	621 (18.4)	2716 (80.5)	3337 (98.9)	< .001
Yes	0 (0.0)	1 (0.0)	0 (0.0)	1 (0.0)	3 (0.1)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	2 (0.1)	0 (0.0)	0 (0.0)	9 (0.3)	28 (0.8)	37 (1.1)	
β-blockers																	
No	123 (3.6)	101 (3.0)	9 (0.3)	112 (3.3)	128 (3.8)	7 (0.2)	9 (0.3)	8 (0.2)	23 (0.7)	2 (0.1)	71 (2.1)	2 (0.1)	7 (0.2)	602 (17.8)	2681 (79.5)	3283 (97.3)	< .05
Yes	5 (0.1)	2 (0.1)	1 (0.0)	2 (0.1)	10 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.1)	0 (0.0)	5 (0.1)	0 (0.0)	0 (0.0)	28 (0.8)	63 (1.9)	91 (2.7)	
Diuretics																	
No	127 (3.8)	100 (3.0)	10 (0.3)	112 (3.3)	135 (4.0)	7 (0.2)	9 (0.3)	7 (0.2)	26 (0.8)	2 (0.1)	70 (2.1)	2 (0.1)	7 (0.2)	614 (18.2)	2700 (80.0)	3314 (98.2)	< .05
Yes	1 (0.0)	3 (0.1)	0 (0.0)	2 (0.1)	3 (0.1)	0 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)	0 (0.0)	6 (0.2)	0 (0.0)	0 (0.0)	16 (0.5)	44 (1.3)	60 (1.8)	
Anti-diabetic Drugs																	
No	122 (3.6)	85 (2.5)	9 (0.3)	95 (2.8)	98 (2.9)	3 (0.1)	7 (0.2)	7 (0.2)	16 (0.5)	1 (0.0)	48 (1.4)	2 (0.1)	4 (0.1)	493 (14.6)	2421 (71.8)	2914 (86.4)	< .001
Yes	6 (0.2)	18 (0.5)	1 (0.0)	19 (0.6)	40 (1.2)	4 (0.1)	4 (0.1)	3 (0.1)	10 (0.3)	1 (0.0)	28 (08)	0 (0.0)	3 (0.1)	137 (4.0)	323 (9.6)	460 (13.6)	
Anti-hyperlipidemic Drugs																	
No	120 (3.6)	91 (2.7)	8 (0.2)	86 (2.5)	91 (2.7)	4 (0.1)	3 (0.1)	7 (0.2)	16 (0.5)	1 (0.0)	40 (1.2)	2 (0.1)	3 (0.1)	470 (13.9)	2260 (67.0)	2730 (80.9)	< .001
Yes	8 (0.2)	12 (0.4)	2 (0.1)	28 (0.8)	47 (1.4)	3 (0.1)	6 (0.2)	3 (0.1)	10 (0.3)	1 (0.0)	36 (1.1)	0 (0.0)	4 (0.1)	160 (4.8)	484 (14.3)	644 (19.1)	

Abbreviations: ACEIs, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CCBs, calcium channel blockers; NSAID, non-steroidal anti-inflammatory drugs.
P value is reported for comparison between CKD-stage.

The medication history of the participants is shown in Table 3. As can be seen, most of the study population were not taking NSAIDs, acetaminophen, angiotensin converting enzyme inhibitors, angiotensin receptor blockers (ARBs), calcium channels blockers, beta-blockers, diuretics, hypoglycemic agents, and anti-hyperlipidemic medications, while NSAIDs (4.9%), ARBs (4.3%), hypoglycemic agents (4.0%), and anti-hyperlipidemic medications (4.8%) were the most consumed medications among CKD patients.

The comparison between the dietary intake of the selected food groups in CKD patients and healthy subjects is shown in Table 4. Compared to healthy subjects, patients with CKD consumed more refined grains and less dairy products.

The demographic data, laboratory findings, and medications, stratified by sex are presented in Table 5. As shown, females had significantly higher age, BMI, HDL, and LDL, as well as, lower

Table 4. Intake of Different Food Groups (Serving per Week) in Healthy Subjects and Patients with CKD

Food Groups	CKD (n = 142)	Healthy (n = 499)	*P*
Refined Grains	55.94 ± 17.388	46.12 ± 18.39	< .05
Whole Grains	12.52 ± 13.59	14.01 ± 15.07	> .05
Legumes	0.85 ± 0.55	1.02 ± 0.57	> .05
Red and Processed Meat	1.48 ± 0.96	2.04 ± 1.02	> .05
White Meat	3.5 ± 1.95	3.56 ± 1.79	> .05
Dairy	6.53 ± 2.16	7.90 ± 2.35	< .05
Vegetables	7.75 ± 3.13	8.58 ± 3.36	> .05
Fruits	5.18 ± 2.42	5.55 ± 2.38	> .05
Healthy Oils (Those containing MUFAs* and PUFAs**)	28.68 ± 11.47	31.41 ± 12.24	> .05
Unhealthy Oils (Those containing saturated and trans fatty acids)	2.72 ± 2.88	2.65 ± 2.94	> .05
Nuts and Seeds	0.72 ± 0.61	0.76 ± 0.85	> .05
Sweets	3.255 ± 2.55	3.64 ± 2.41	> .05

*Monounsaturated fatty acids
**Polyunsaturated fatty acids

Table 5. Descriptive Statistics for Risk Factor Based on Gender Groups

Variables	Female	Male	*P*
Demographic Variables			
Age, y	48.08 ± 13.59	51.09 ± 14.62	< .001
Marital status (n (%))			
Married	1669 (49.5)	1215 (36.0)	< .001
Single	331 (9.8)	159 (4.7)	
Education (n (%))			
College Education	387 (11.5)	261 (7.7)	
Illiterate	323 (9.6)	127 (3.8)	< .001
School Education	1290 (38.2)	986 (29.2)	
Smoking			
No	1910 (56.6)	926 (27.4)	< .001
Yes	90 (2.7)	448 (13.3)	
Alcohol Use			
No	1974 (58.5)	1275 (37.8)	< .001
Yes	26 (0.8)	99 (2.9)	
Opioid Use			
No	1981 (58.7)	1285 (38.1)	< .001
Yes	19 (0.6)	89 (2.6)	
Clinical Variables			
Body Mass Index, kg/m^2	27.15 ± 4.84	26.33 ± 4.69	< .001
Systolic Blood Pressure, mmHg	117.36 ± 18.69	127.09 ± 19.04	< .001
Diastolic Blood Pressure, mmHg	65.17 ± 27.88	68.74 ± 29.05	< .001
Waist to Hip Ratio	0.912 ± 1.53	0.934 ± 0.14	> .05
Physical Activity	6.71 ± 1.22	7.09 ± 1.33	< .001

Table 5. Continued

Variables	Female	Male	*P*
Laboratory Variables			
Triglyceride (mg/dL)	147.56 ± 63.49	164.16 ± 75.12	< .001
Total Cholesterol (mg/dL)	169.02 ± 47.78	175.05 ± 52.24	< .05
High density lipoprotein (mg/dL)	54.06 ± 11.02	46.53 ± 9.51	< .001
Low density lipoprotein (mg/dL)	97.54 ± 31.22	95.03 ± 29.46	< .05
Fasting blood Glucose (mg/dL)	87.96 ± 23.37	89.30 ± 24.91	> .05
Drug History			
NSAIDs			
No	1330 (39.4)	1122 (33.3)	< .001
Yes	670 (19.9)	252 (7.5)	
Acetaminophen			
No	1888 (56.0)	1349 (40.0)	< .001
Yes	112 (3.3)	25 (0.7)	
ACEIs			
No	1983 (58.8)	1365 (40.5)	> .05
Yes	17 (0.5)	9 (0.3)	
ARBs			
No	1693 (50.2)	1192 (35.3)	> .05
Yes	307 (9.1)	182 (5.4)	
CCBs			
No	1979 (58.7)	1358 (40.2)	> .05
Yes	21 (0.6)	16 (0.5)	
B Blockers			
No	1945 (57.6)	1338 (39.7)	> .05
Yes	55 (1.6)	36 (1.1)	
Diuretics			
No	1962 (58.2)	1352 (40.1)	> .05
Yes	38 (1.1)	22 (0.7)	
Anti-diabetic Drugs			
No	1707 (50.6)	1210 (35.9)	< .05
Yes	293 (8.7)	164 (4.9)	
Anti-hyperlipidemic Drugs			
No	1573 (46.6)	1157 (34.3)	< .001
Yes	427 (12.7)	217 (6.4)	

Abbreviations: ACE, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; NSAID, non-steroidal anti-inflammatory drugs.

SBP, waist to hip ratio, and physical activity levels (*P* value < .05 for all). Moreover, they were more likely to be single, illiterate, non-smoker, non-opioid user, and drank less alcohol (*P* value < .05).

Table 6 illustrates the association between various study parameters and risk of CKD. Logistic regression analysis demonstrated that older age, higher BMI and SBP, female gender, and being single, illiterate, and/ or smoker were significantly associated with higher risk of CKD. Likewise, increased risk of CKD was associated with lower levels of HDL, LDL, waist to hip ratio, and physical activity. Additionally, the relationship between the medications such as ARBs, beta-blockers, and hypoglycemic and anti-hyperlipidemic agents and lower odds of CKD was demonstrated in our study.

DISCUSSION

The current study represents the prevalence of CKD and its risk factors in Isfahan province, Iran. The results illustrated an overall prevalence of 18.5% for CKD. Compared to the results of the latest relevant meta-analysis study, which estimated the global prevalence of CKD as 13.4%,[2] its prevalence rate seems to be even higher in Iran. Due to high prevalence of CKD in this area, careful monitoring of general population, especially individuals who are at-risk for CKD, is imperative.

A pilot community-based CKD screening program in commercial centers in Riyadh, Saudi

Table 6. ODDs Ratio for Risk Factors

Variables	Odds Ratio	95% CI for EXP (B)		*P*
		Lower	Upper	
Demographic Variables				
Age, y (n (%))				
18 to 44	0.204	0.132	0.299	< .001
45 to 64	0.244	0.168	0.355	< .001
65 to 74	0.507	0.336	0.766	< .05
> 75				
Gender (n (%))				
Female	1.319	1.101	1.579	< .05
Male				
Marital status (n (%))				
Single	1.335	1.058	1.683	< .05
Married				
Education (n (%))				
College Education	0.762	0.596	0.973	< .05
Illiterate	1.912	1.519	2.403	< .001
School Education				
Smoking				
Yes	1.529	1.176	1.988	< .05
No				
Alcohol Use				
Yes	1.477	0.879	2.481	> .05
No				
Opioid Use				
Yes	1.700	0.946	3.058	> .05
No				
Clinical Variables				
Body Mass Index	1.030	1.013	1.050	< .05
Systolic Blood Pressure, mm/Hg	1.018	1.014	1.022	< .001
Diastolic Blood Pressure, mm/Hg	1.005	1.002	1.008	< .05
Waist to Hip Ratio	0.995	0.916	1.079	> .05
Physical Activity	0.900	0.841	0.962	< .05
Laboratory Variables				
Triglyceride, mg/dL	1.000	0.999	1.002	> .05
Total Cholesterol, mg/dL	1.000	0.998	1.002	> .05
HDL, mg/dL	0.989	0.980	0.997	< .05
LDL, mg/dL	0.996	0.994	0.999	< .05
FBS, mg/dL	1.011	1.008	1.014	< .001
Drugs History				
NSAIDs				
Yes	0.950	0.781	1.156	> .05
No				
Acetaminophen				
Yes	0.776	0.515	1.170	> .05
No				
ACEIs				
Yes	0.513	0.222	1.186	> .05
No				
ARBs				
Yes	0.479	0.386	0.596	< .001
No				
CCBs				
Yes	0.711	0.334	1.515	> .05
No				

Table 6. Continued

Variables	Odds Ratio	95% CI for EXP (B)		*P*
		Lower	Upper	
B Blockers				
Yes	0.505	0.321	0.795	< .05
No				
Diuretics				
Yes	0.625	0.351	1.116	> .05
No				
Anti-diabetic Agents				
Yes	0.475	0.380	0.593	< .001
No				
Anti-hyperlipidemia Medications				
Yes	0.629	0.513	0.772	< .001
No				

Arabia, showed a CKD prevalence of 5.3% in young population. CKD-EPI glomerular filtration rate equation was used for calculating GFR.[17] In contrast to our study, they used urine dipstick for the detection of microalbuminuria, while serum creatinine concentration was measured by the Jaffe reaction, similar to our methodology. The authors also used the National Kidney Foundation (NKF) criteria for the definition and diagnosis of CKD. In another population-based survey of Chronic Kidney Disease in Turkey, the overall prevalence of CKD was estimated to be 15.7%.[18] In contrast to the present study, they used a simplified version of the MDRD formula for calculation of eGFR and did not consider hematuria in their criteria for the diagnosis of CKD. The age variations between studies, and also disparities in the distributions of major risk factors (central obesity, diabetes, and hypertension) could explain the difference in the prevalence found in different studies.[19]

Several studies investigated the CKD prevalence in Iran, which have expressed different results. Bouya *et al.* conducted a systematic review and meta-analysis and reported that the overall prevalence of CKD was 15.1% in Iran.[7] A cross-sectional study, conducted by Saber *et al.* in 2019, reported the prevalence of CKD in 988 adults (15 to 75 years) in Kerman city as 30.9%.[20] In another study by Spanalo *et al.*, a total of 11,409 participants were selected from all residents aged 40 to 75 from 326 villages of Golestan province and a sample from Gonbad city. Twenty-five percent of the individuals in this group showed low eGFR.[(21)] However, they did not use microalbuminuria for the diagnosis and classification of CKD in their study. Additionally, the prevalence of CKD was estimated as 4.6% in the general population of a rural area in Isfahan by Ebrahimi *et al.*[22] One probable reason for the variations in the results of these studies and their differences compared to our study, could be the different methods for determining eGFR. Most of these studies used the MDRD equation, which underestimates GFR. Also, neither of these documents included hematuria in their criteria. The characteristics of the population of our study are different from other investigations, which could be another reason for the variations in result.

As reported in several surveys from Norway, Italy, and China, CKD in early stages is also predominant in Isfahan province.[23-25] Meanwhile, the prevalence of CKD stages 3–5 (moderate to advanced) is remarkably higher in the United States.[25] The higher prevalence of impaired kidney function in the United States compared to other countries can be due to the impact of associated risk factors including hypertension, diabetes, obesity, and CVD which are more prevalent in those areas.

We found a significant correlation between female gender, age, BMI, SBP, smoking, low educational level, use of NSAIDs, and higher intake of refined grains and lower consumption of dairy and development of CKD, similar to the previous studies.[7, 26, 27] However, lower waist-to-hip ratio (WHR) was related to higher risk of CKD in our study, which was unexpected. This can be explained by the fact that about two-thirds of CKD cases in our study were females (64.6%), among whom WHR was lower; whereas males with higher WHR comprised about one-third of CKD cases (35.4%). Moreover, we found that CKD

was associated with marital status, which is not unexpected considering the emotional and social support that can be provided by the partner.[28] In addition, higher quality of life, healthier lifestyle and behaviors,[29] and better medical treatment[30] were among other benefits of being married. However, the exact impact of marital status on CKD prevalence is not clear.

The results obtained from this study could be implicated in major public health issues. They ascertain determine that employing weight loss programs and improving cardio-metabolic risk factors by physical activity and nutritional interventions could decrease the possibility of reduced kidney function. It should be taken into account that the prevalence of impaired kidney function is expected to increase in the future. Due to population aging in Iran and increased elderly population from 7.27% in 2006 to 8.65% in 2016, it is predicted that elderly people may compose10.5 and 21.7% of the CKD patients in 2025 and 2050, respectively.[31] Aging is accompanied by increase in the prevalence of non-communicable diseases such as diabetes.[32] Higher risk of cardiovascular events and/ or early death and increase in the end-stage kidney disease burden are the two main consequences of increased number of CKD cases.[33] Thus, it appears that actions for lifestyle and risk factor modification are imperative to diminish the risk of CKD.

We encountered several limitations in our study: 1) Overestimation of the prevalence of CKD is probable, since we used single measurements for all CKD indicators; 2) As the study was conducted in Isfahan, the results could not be generalized to the whole nation; 3) Females constituted the majority of our study population; 4) Subjects were selected from governmental health care centers which mostly include people with health issues, house wives, elderly, unemployed individuals, as well as people with low socioeconomic status. These could have confounded the results; and 5) Imaging is another important method for CKD diagnosis, which was not used in this study.

CONCLUSION

Our study revealed an overall CKD prevalence of 18.5% in Isfahan, one of the largest cities in Iran, and also showed that smoking, older age, higher BMI and SBP, female sex, marital status, and low educational levels were significantly associated with higher risk of CKD. Additionally, increased risk of CKD is linked to decreased HDL and LDL levels and low waist-to-hip ratio and physical activity. The results of this study can be used to improve the monitoring of CKD patients in a larger scale and to identify the challenges faced when conducting prevalence studies. We recommend a nationwide prevalence study in Iran, for early diagnosis and management of the disease by healthcare personnel and facilities.

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