

Original Article

Prevalence of Chronic Kidney Disease and its Associated Risk Factors: The First Report from Iran Using Both Microalbuminuria and Urine Sediment

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Abstract

Background: The incidence of major risk factors of chronic kidney disease (CKD) in the world is on the rise, and it is expected that this incidence and prevalence, particularly in developing countries, will continue to increase. Using data on urinary sediment and microalbuminuria, we aimed to estimate the prevalence of CKD in northeast Iran.

Methods: In a cross-sectional study, the prevalence of CKD in a sample of 1557 regionally representative people, aged ≥ 18 years, was analyzed. CKD was determined based on glomerular filtration rate (GFR) and microalbuminuria. Life style data, urine and blood samples were collected. Urine samples without any proteinuria in the initial dipstick test were checked for qualitative microalbuminuria. If the latter was positive, quantitative microalbuminuria was evaluated.

Results: 1557 subjects with a mean age of 56.76 ± 12.04 years were enrolled in this study. Based on the modification of diet in renal disease (MDRD) equation, 137 subjects (8.89%) were categorized as CKD stages III-V. Based on urine abnormalities, the prevalence of combined CKD stages I and II was 10.63%, and based on macro- and microalbuminuria it was 14.53%. The prevalence of CKD was significantly associated with sex, age, marital status, education, diabetes mellitus (DM), hypertension (HTN), ischemic heart disease (IHD), waist to hip ratio, myocardial infarction (MI), and cerebrovascular accident (CVA).

Conclusion: CKD and its main risk factors are common and represent a definite health threat in this region of Iran. Using and standardizing less expensive screening tests in low resource countries could be a good alternative that may improve the outcome through early detection of CKD.

Keywords: Chronic disease, Iran, kidney, nephelometry

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Introduction

The incidence of end-stage renal disease (ESRD) is dramatically increasing worldwide.¹ Most patients with kidney problems visit their physicians in the late stages of the disease. Progression from mild to moderate kidney disease to ESRD may be halted or slowed when kidney damage is detected and appropriate treatment is started during the early stages. Kidney damage is frequently asymptomatic but can be suspected in the presence of proteinuria, hematuria, or a reduced glomerular filtration rate (GFR).² While previously different criteria such as abnormal

urine sediment and increased serum creatinine level were used to define chronic kidney disease (CKD), in 2002 the Kidney Disease Outcomes Quality Initiative (KDOQI) proposed a classification system based on changes in the GFR. In this system albuminuria is an essential element in the diagnosis of mild CKD (stages I and II).³ According to the Kidney Early Evaluation Program (KEEP 2.0) in the US, 3% of participants reported a history of kidney disease. A total of 18% had hematuria and 13% had pyuria. Microalbuminuria was found in 29% of participants.⁴

Proteinuria of less than 150 mg per liter could not be identified with routine dipsticks. Therefore, more sensitive tools such as urine nephelometry are used to detect microalbuminuria. In urine nephelometry, albumin > 30 mg/g are considered abnormal. Population-based studies on the prevalence of kidney damage, particularly in its earlier stages and diagnosed with microalbuminuria, are limited in countries other than high-income countries.⁵⁻⁸ This is in part related to the difficulty of applying quantitative methods for the detection of albuminuria in large epidemiological studies in low- to middle-income countries like Iran.

We previously reported the prevalence of moderate to severe CKD (stages III-V) based on GFR in Golestan Province.⁹ In this study, we provided data on urinary sediment and microalbuminuria and extended our previous observations to milder stages of CKD (stages I-II).

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Table 1. Distribution of demographic variables, BMI, and medical history among groups of interest.

Characteristic	Number (%)	Characteristic	Number (%)
All participants	1557 (100)	Marital Status	
Women	829 (53.24)	Married	1330 (85.42)
Men	728 (46.76)	Single	44 (2.83)
Age (years)		Widowed/divorced	183 (11.75)
< 30	82 (5.27)	Education	
30–39	62 (3.98)	No school	935 (60.05)
40–49	86 (5.52)	Primary school	350 (22.4)
50–59	672 (43.16)	Middle school	69 (4.4)
60–69	435 (27.94)	High school	139 (8.9)
≥ 70	220 (14.13)	University	64 (4.1)
Ethnicity		BMI	
Sistani	583 (37.44)	< 18.5	57 (3.66)
Turkmen	409 (26.27)	18.5–24.9	1103 (70.8)
Fars	347 (22.29)	25–29.9	331 (19.9)
Other	218 (14.00)	≥ 30	86 (5.5)
Hypertension		Diabetes	
Self-reported	393 (25.2)	Self-reported	239 (15.3)
Sys ≥ 140 or Dias ≥ 90 mmHg	673 (43.2)	FBS ≥ 110 mg/dL	328 (21.07)
Any criteria	792 (50.8)	Any criteria	414 (26.6)
Ischemic heart disease	177 (11.3)	Myocardial infarction	49 (3.1)

Table 2. MDRD-based glomerular filtration rate by sex and age.

All participants	Total no.	Mean age (SD)	GFR < 15	GFR: 15–29	GFR: 30–59	GFR: 60–89	GFR ≥ 90
Women	1542	56.76 (12.04)	4 (.26)	4 (.26)	129 (8.37)	1043 (67.64)	362 (23.48)
Men	821	58.08 (10.53)	4 (0.49)	2 (0.24)	47 (5.72)	540 (65.77)	228 (27.77)
Age (years)	721	55.25 (13.4)	0 (0.0)	2 (0.28)	82 (11.37)	503 (69.76)	134 (18.59)
<30	81	23.1 (3.5)	0 (0.0)	0 (0.0)	1 (1.23)	17 (20.99)	63 (77.78)
30–39	62	34.22 (2.8)	0 (0.0)	0 (0.0)	2 (3.23)	46 (74.19)	14 (22.58)
40–49	86	5 (3.1)	0 (0.0)	0 (0.0)	1 (1.16)	69 (80.23)	16 (18.60)
50–59	666	54.67 (2.79)	1 (0.15)	2 (0.3)	20 (3.00)	480 (72.07)	163 (24.47)
60–69	432	63.7 (3.0)	1 (0.23)	2 (0.46)	62 (14.35)	283 (65.51)	84 (19.4)
≥ 70	220	72.4 (2.41)	2 (0.93)	0 (0.0)	43 (20.0)	148 (68.84)	22 (10.23)

BMI = body mass index (kg/m²); GFR = glomerular filtration rate (ml/min/1.73 m²); MDRD = Modification of Diet in Renal Disease; SD = standard deviation. Values are numbers (percentages) of participants unless stated otherwise.

Materials and Methods

The subject enrollment method has been described in detail in our previous report.⁹ In brief, all men aged 50 to 79 and women aged 55 to 79 years who resided in the city of Kalaleh and were invited to participate in the double-blind randomized placebo-controlled pilot trial of the effects of fixed-dose combination therapy ('polypill') on cardiovascular risk factors in Kalaleh (n = 1488; participation rate 70%),¹⁰ regardless of their eligibility for the trial, were enrolled in this study. To have representative samples of the adult population, the study participants were contacted by phone and all individuals aged 18 years or older in their household were invited to participate (participation rate > 95%). We recruited a total of 3613 subjects from April 2007 to January 2009. Questionnaire data, and urine, and blood samples were collected from all participants. For this study we used data of first 1557 subjects, for whom microalbuminuria data were available along with urine sediment. For the rest of the study quantitative microalbuminuria kit was not available due to sanctions on Iran.

The study protocol and the informed consent were approved by the "Ethics Review Committee" of the "Digestive Disease Research Center" of "Tehran University of Medical Sciences". Written informed consent was obtained from all participants.

Demographic data, habits, and history of medical conditions including diabetes mellitus (DM), hypertension (HTN), ischemic heart disease (IHD), and myocardial infarction (MI) were collected by face-to-face interviews using a structured questionnaire. Weight and height were measured. Systolic and diastolic blood pressures

were obtained twice within a 20 minute interval for both arms during the interview, however, only measurements of the right arm were considered for further analyses. Trained physicians conducted the interviews and physical examinations.

Waist circumference was measured at the umbilical level as well as hip circumference at the maximal level over light clothing. Waist to hip ratio was calculated by dividing waist to hip circumference. Weight was recorded using scales (with precision of up to 50 g). Height was measured using a tape stadiometer. Body mass index (BMI) was calculated by dividing weight (in kg) by squared values of height (in meters). In order to reduce inter-observer variability, only one of the research team members performed all the anthropometric measurements.

Fasting blood samples and one-spot urine samples were collected from all participants. Blood samples were drawn by a nurse, after at least ten hours of overnight fasting. Serum was separated and kept in 70°C freezers in the study center for a maximum period of three months. The samples were transported in dry ice to a reference laboratory where biochemical analysis was performed. The laboratory analyses were done within a few days after arrival with endpoint enzymatic photometric method using a Hitachi 902 auto-analyzer.

Fasting blood glucose was measured by the glucose oxidase method (Pars Azmon Inc., Iran) with an inter-assay coefficient of variation (CV) of 3% and an intra-assay CV of 0.8%. Total cholesterol (TC) and triglyceride (TG) levels were measured using enzymatic colorimetric kits (Pars Azmon, Inc.) with an inter-assay CV of 2% and an intra-assay CV of 0.5% for TC, an inter-assay CV

Table 3. Univariate analysis of effect of variables on CKD.

Variable	CKD stages I-V (%) n = 361	GFR ≥90 (%) n = 1181	Crude OR (95% CI)	Variable	CKD stages I-V (%) n = 361	GFR ≥90 (%) n = 1181	Crude OR (95% CI)
Sex				Diabetes			
Women	190 (52.6)	650 (55.04)	Reference	Self-reported	95 (26.3)	143 (12.1)	2.59 (1.93–3.47)
Men	171 (47.3)	531 (44.96)	0.73 (0.58–0.93)	FBS ≥110 mg/ dL	126 (34.9)	202 (17.1)	2.59 (1.99–3.38)
Age (years)				Any criteria	145 (40.2)	268 (22.7)	2.28 (1.77–2.93)
< 30	11 (3.05)	70 (5.93)	Reference	Waist to hip ratio			
30–39	8 (2.22)	54 (87.10)	0.94 (.35–2.50)	Below25% quartile	75 (20.78)	309 (26.16)	Reference
40–49	12 (13.95)	74 (6.27)	1.03 (0.42–2.49)	25–50% quartile	84 (23.27)	303 (25.66)	1.14 (0.80–1.61)
50–59	113 (31.30)	553 (46.82)	1.30 (0.66–2.53)	50–75% quartile	97 (26.87)	318 (26.93)	1.25 (0.89–1.76)
60–69	133 (36.84)	299 (25.32)	2.83 (1.45–5.51)	Above75% quartile	105 (29.09)	251 (21.25)	1.72 (1.22–2.42)
≥ 70	84 (23.27)	131 (11.09)	4.08 (2.04–8.15)	IHD	64 (17.73)	112 (9.48)	2.05 (1.47–2.86)
Ethnicity				BMI			
Sistani	122 (33.8)	454 (38.4)	Reference	<18.5	7 (2)	47 (4)	0.52 (0.23–1.18)
Turkmen	91 (25.2)	315 (26.7)	1.07 (0.79–1.46)	18.5–24.9	250 (69.2)	844 (71.5)	Reference
Fars	93 (25.8)	250 (21.2)	1.38 (1.01–1.88)	25–29.9	86 (23.8)	222 (11.8)	1.07 (0.81–1.42)
Others	55 (15.2)	162 (13.7)	1.26 (0.87–1.82)	≥ 30	18 (5)	68 (5.7)	1.25 (0.92–1.70)
Marital status				HTN			
Married	296 (82.0)	1021 (86.5)	Reference	Self-reported	146 (40.44)	245 (20.75)	2.59 (2.01–3.34)
Widowed /Divorced	61 (16.9)	122 (10.3)	1.7 (1.23–2.40)	Sys ≥140 or Dias ≥90 mmHg	208 (57.62)	459 (38.87)	2.06 (1.01–4.18)
Single	4 (1.1)	38 (3.2)	0.36 (0.12–1.02)	Any criteria	237 (65.65)	547 (46.32)	2.21 (1.73–2.83)
Education				MI	18 (4.99)	31 (2.62)	1.94 (1.07–3.52)
No school	229 (63.4)	695 (58.8)	Reference	CVA	14 (3.88)	23 (1.95)	2.14 (1.33–3.46)
Primary school	85 (23.5)	262 (22.2)	0.35 (0.23–0.57)	Smoking	50 (13.85)	191 (16.17)	0.83 (0.59–1.16)
Middle school	16 (4.4)	53 (4.5)	0.11 (0.05–0.23)	Opium	46 (12.74)	161 (13.63)	.92 (0.65–1.31)
High school	19 (5.3)	120 (10.2)	0.04 (0.02–0.08)	Nass	21 (5.82)	65 (5.50)	1.06 (0.63–1.76)
University	12 (3.3)	51 (4.3)	0.05 (0.02–0.14)	Alcohol	1 (0.28)	9 (0.76)	0.36 (0.04–2.86)

Table 4. Difference between mean of biochemical factors and waist to hip ratio based on CKD status.

Variable	CKD positive n = 361	CKD negative n = 1181	P-value for student t-test
	Mean (SD)	Mean (SD)	
Uric acid	5.23 (1.54)	5.22 (7.39)	0.97
Cholesterol	198.96 (50.84)	190.21 (53.38)	0.005
Triglyceride	163.02 (100.13)	147.59 (108.66)	0.01
HDL	45.65 (12.30)	47.38 (13.30)	0.02
LDL	115.30 (33.95)	108.58 (42.79)	0.006
ESR	19.74 (14.17)	14.03 (9.90)	0.000
HB	12.56 (1.70)	12.67 (1.66)	0.27
FBS	119 (2.82)	102.06 (1.23)	0.0000
Waist to hip ratio	0.95 (0.004)	0.93 (0.002)	0.0016

of 1.6% and an intra-assay CV of 0.6% for TG. Serum creatinine levels were assessed according to the standard colorimetric Jaffe-Kinetic reaction method (Pars Azmon Inc., Iran), with an inter-assay CV of 2.5%, an intra-assay CV of 1.9%, and a sensitivity of 0.2 mg/dL. The assay range was 18–1330 μmol (0.2–15 mg/dL). Assay performance was monitored after every 30 tests using the control serum, TrueLab N (Lot. no. 11382; Pars Azmon, Inc., Iran) for normal ranges and TrueLab P (Lot. no. 11383; Pars Azmon, Inc., Iran) for pathological ranges. In subjects with abnormal urine sediment and creatinine levels, these parameters were rechecked after at least three months.

Urine samples were sent to a local reference laboratory the morning of collection. When samples showed abnormal urine findings (white blood cells > 5 or red blood cells > 3 per high-power field, or protein ≥ trace), a visit to a nephrologist and complementary tests including urine culture, renal ultrasound, and additional tests (depending on findings) were considered. Protein/creatinine ratio was calculated for samples with proteinuria. For samples with no urine sediment abnormality, the presence of microalbuminuria was qualitatively examined and if the test was positive, albumin was then measured quantitatively using the nephelometric method. Because of the sanctions against Iran and the unavailability of

Table 5. CKD prevalence using microalbuminuria versus urine sediment.

Different groups & different screening protocol	Number of participants	Mean age (SD)	CKD stages I-II (GFR > 60 and albuminuria) N (%)	CKD stages I-II (GFR > 60 and abnormal sediment) N (%)	CKD stages III-V N (%)	CKD stages I-V based on abnormal sediment N (%)
Group of interest (our study group)	1557	56.73 (12.03)	221 (14.53)	164 (10.63)	137 (8.89)	301 (19.52)*
Remainder	2056	34.06 (10.24)	ND**	180(8.78)	28 (1.37)	208 (10.15)
Total	3613	43.84 (15.76)	ND**	344 (9.57)	165 (4.60)	509 (14.17)

*CKD prevalence in group of interest based on microalbuminuria = 14.53 + 8.89 = 23.42%; **ND = Not done.

qualitative microalbuminuria kits, qualitative evaluation of microalbuminuria was performed only in the 1557 subjects with normal urine sediment findings.

Definitions

For this study, GFR was estimated from the abbreviated prediction equation provided by the Modification of "Diet in Renal Disease (MDRD)" study as follows:

$$\text{GFR} = 186 \times (\text{SCr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$$

We classified CKD stages I-II through two modalities:

1) Based on macro and microalbuminuria: GFR > 60 mL/min per 1.73 m² and microalbuminuria \geq 30 mg or \geq trace positive proteinuria.

2) Based on urine sediment: GFR > 60 mL/min per 1.73 m² and abnormal urine sediment (described above).

We defined stages III CKD as a GFR of 31–60 mL/min and stage IV as a GFR of 16–30 mL/min; and stage V as a GFR \leq 15 mL/min per 1.73 m².

BMI was categorized in four groups of < 18.5 kg/m², 18.5 to 24.9, 25 to 29.9 and \geq 30 kg/m². Abnormal waist circumference was set as \geq 102 cm in men and \geq 88 cm in women according to the "Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults". Opium usage, cigarette smoking, and nass (a chewing tobacco mixture) were defined as being used at least once a week for six months. DM was defined according to the criteria of the last statement of the "American Diabetes Association (ADA)" as fasting plasma glucose \geq 110 mg/dL, including patients who had known cases of diabetes and were using insulin or oral glucose-lowering agents.

We have defined presence or absence of HTN and DM by three different ways:

- 1) Self-reported (data which was obtained by the questionnaire),
- 2) Measured (data which was obtained through measurement), and
- 3) Both 1 and 2.

Classification of measured blood pressure was based on "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNCVII)".

Results

Initially there were 1557 enrolled subjects in this study, with a mean age of 56.76 \pm 12.04 (female: 55.25 \pm 13.40 and male: 58.08 \pm 10.53 years) who were assumed to be one group of interest. The

demographic characteristics of these subjects are presented in Table 1.

We calculated the awareness rate of the interest group with aforementioned medical problems by dividing the self-reported numbers to the sum of measured and self-reported data. Only 10% of patients with kidney disease, 57.6% with diabetes, and 49.8% with HTN were aware of their illness.

A family history of HTN was noted in 20.88% of the subjects, compared to family history of DM (13%), IHD (5.38%), MI (6.87%) and cerebrovascular accident (CVA; 6.74%). Alcohol consumption was rare (0.65%), while 15.63% of the subjects smoked cigarettes, 13.42% used opium and 5.58% used nass.

The distribution of GFR classified groups according to demographic and health characteristics are presented in Table 2. Among the study population, the mean creatinine level was 0.97 \pm 0.51 mg/dL, and the mean estimated GFR based on the MDRD formula was 80.2 \pm 34.52 mL/min/1.73 m². High serum creatinine in men (> 1.3 mg/dL) was detected in 36 subjects, and in 48 women (> 1.1 mg/dL).

Using a logistic regression analysis the prevalence of CKD was associated with sex, age, marital status, education, DM, HTN, IHD, waist to hip ratio, MI and CVA (Table 3). In multivariate analysis, sex, age, DM, HTN, and IHD showed a significant association with CKD. There was a significant difference between mean cholesterol, TG, HDL, LDL, ESR, FBS, and waist to hip ratio of CKD patient and healthy subjects (Table 4).

Table 5 shows CKD prevalence using macro- and micro-albuminuria versus urine sediment. The GFR measurement based on the MDRD equation is used as a universal protocol to categorize CKD stages III-V. Based on dipstick and urine analysis, 5.7% had proteinuria (5.4% of females, 6% of males), 3.7% had pyuria (5.4% of females and 2.3% of males) and 5.5% had hematuria (6.6% of females, 4.6% of males). Among individuals with pyuria, 72% had a positive urine culture but only 35% had a colony count more than 100 000 (Table 5).

Based on the MDRD equation a total of 137 subjects (8.89%) and based on the Cockcroft-Gault a total of 219 subjects (14.2%) were categorized as CKD stages III-V. Using the MDRD equation with macro- and micro-albuminuria classification, 23.42% (stages: I, 3.8%; II, 10.7%; III, 8.37%; IV, 0.26; and V, 0.26%) had CKD. With urine sediment, 19.52% (stages: I, 2.2%; II, 8.1%; III, 8.37%; IV, 0.26; and V, 0.26%) had CKD.

During the study, 500 participants (out of 3613) had abnormal urine sediment and/or elevated serum creatinine. There were 200 who had further evaluations by a nephrologist, including repeating the abnormal test sonography and/or radiography, and on rare occasion's, admission to a hospital. The most prevalent diagnoses

between these subjects were Hypertension, diabetes mellitus, obesity and X syndrome.

Discussion

Due to increased awareness of people about CKD and early detection and prevention programs implemented in developed countries, the incidence of ESRD has shown a small downward trend.¹¹⁻¹² However the total number of individuals worldwide with CKD is still high and estimated at 500,000,000 people.

In our study, 4.6% of the population of Kalaleh has stage III-V CKD, which was consistent with the result of the NHANES study in which a CKD prevalence of 4.7% was reported in the US.¹³ However, in different parts of the world this figure varies between 2.5% in China,⁶ 6.9% in Taiwan,¹⁴ 7.8% in Congo,¹⁵ and 10.9% in Australia.² In a study of over 17000 people from Iran, a prevalence of 6% to 17% in different provinces were recorded.¹⁶ In the capital city of Tehran, the prevalence of CKD stages III-V among 32000 taxi drivers was found to be 6.5% in men and 13.7% in women.¹⁷ In another study in Tehran, with over ten thousand surveyed, a very high number of 19% was noted.¹⁸

For the definition of CKD stages I and II, different screening protocols (estimated GFR plus macro- and microalbuminuria, and abnormal urine sediment) were used. In this study, we compared the CKD prevalence among our subjects based on two modalities. Taking into account the macro- and microalbuminuria in our evaluation strategy showed us a higher percent of CKD compared to using only abnormal urine analysis and GFR measurement (19.52% vs. 23.41%). Such an increase in detection of CKD by microalbuminuria measurement is an expected finding since the latter is the most precise way of determining CKD. Similar to our study, analysis of NHANES data from 4101 individuals from 1999 to 2000 (using dipstick albuminuria) showed a CKD prevalence of 1.7% in males and 0.9% in females. These figures rose to 7.3% and 10.4% when the quantitative measurement of microalbuminuria was used as the modality for CKD determination.¹⁹

Though the relation between microalbuminuria to cardiovascular and renal morbidity and mortality has been well documented by several studies,²⁰⁻²¹ we are not aware of studies evaluating a similar relationship with abnormal urine sediment in CKD patients. In concordance with previous reports only 25% (26/104) of our CKD stage III had microalbuminuria. The numbers were also similar for abnormal urine sediment 28.5% (44/154). The deleterious renal and cardiac effect of microalbuminuria is well known. In fact, in Multiple Risk Factor intervention and CARE trials²⁰ and the Framingham Offspring cohort²¹ it has been documented that regardless of the stages of CKD, the main hazard for developing ESRD and cardiovascular events comes from albuminuria. We are not aware of long-term clinical consequences due to abnormal urine sediment in CKD, which should be investigated in the future. In our study, diabetes, HTN, obesity and metabolic syndrome accounted for 70% of the causes of CKD in subjects with abnormal screening tests that underwent further evaluation. These figures are similar to the results in the US presented in Figure 1.

In the NHANES study, the prevalence of moderate or severe decreased kidney function in the age group ≥ 70 years was reported to be around 20.6%, which was substantial even in the absence of diabetes or HTN (10.8%).¹³ Accordingly, we found a higher percent of CKD among older individuals (age ≥ 50 years) than younger (age 20–40 years) in this study (23.27% vs. 3.05%).

In the general population of Kalaleh, type two DM had a prevalence of 17.5% compared to the worldwide reported figure of 5%. The high prevalence of diabetes in Kalaleh could be explained by the high rate of BMI > 25 (60%), lack of physical activity, and possibly genetic and racial background. In the KEEP study, 27% of people with CKD had diabetes, a figure similar to our study. However, the prevalence of HTN was much higher in our study group compared to KEEP (50% vs. 17%), while obesity was lower (27% vs. 44%).⁴ Despite finding an association between CKD and several known risk factors that included HTN, DM, IHD, MI, and waist to hip ratio, no association existed between CKD and BMI. The correlation between CKD and waist to hip ratio and not BMI is plausible since this ratio is a more representative marker of metabolic syndrome than BMI.

One interesting finding of our study was the marked difference in our subjects' awareness of their presence or absence of CKD compared with diabetes and HTN. This was partly due to the long history of successful public education about diabetes and HTN compared to renal disease in Iran, as well as the lack of knowledge among health care workers regarding the importance of screening patients for CKD.

It is worth noting the limitations and strengths of the current study. First, estimating the GFR from the serum creatinine level has well-recognized limitations, including substantial variation in creatinine production by age, sex, and race.²² To minimize the impact of these limitations, we used the MDRD equation which has an increased precision of GFR estimation. As expected, the Cockcroft-Gault equation underestimates GFR, so the prevalence of CKD based on this method is higher compared to the MDRD equation. Unfortunately, we did not have access to the calibration of serum creatinine values or to the laboratory that generated data for the development of this equation. Also, microalbuminuria was measured only in 40% of participants (n = 1557) due to unavailability of the kit in Iran. This resulted in the complete data only in a subgroup of participants not representative of the total group, because this group was older and had more co-morbidity. The strength of this study was that we were able to compare CKD prevalence based on two screening methods, macro and microalbuminuria and abnormal urine sediment. We showed that the prevalence of CKD was 4% higher using the former method.

In this study, we found a similar prevalence of CKD in Kalaleh, as well as its main risk factors (age, diabetes, HTN, metabolic syndrome, and obesity) compared with developed countries. Simple urine analysis plus creatinine measurement are easily available and could diagnose the majority of our patients with CKD. Perhaps in low resource countries this can be recommended as a minimum for screening purposes, and routine use of microalbuminuria be used in a high-risk population.

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References

1. Bommer J. Prevalence and socio-economic aspects of chronic kidney disease. *Nephrol Dial Transplant*. 2002; **17** (suppl 11): 8 – 12.
2. Chadban SJ, Briganti EM, Kerr PG, Dunstan DW, Welborn TA, Zimmet PZ, et al. Prevalence of kidney damage in Australian adults: the AusDiab Kidney Study. *J Am Soc Nephrol*. 2003; **14** (suppl 2): S131–S138.
3. Hallan SI, Orth SR. The KDOQI 2002 classification of chronic kidney disease: for whom the bell tolls. *Nephrol Dial Transplant*. 2010; **25**: 2832 – 2836.
4. Brown WW, Peters RM, Ohmit SE, Keane WF, Collins A, Chen SC, et al. Early detection of kidney disease in community settings: the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis*. 2003; **42**: 22 – 35.
5. Amato D, Alvarez-Aguilar C, Castaneda-Limonos R, Rodriguez E, Avila-Diaz M, Arreola F, et al. Prevalence of chronic kidney disease in an urban Mexican population. *Kidney Int Suppl*. 2005; (**97**): S11–S17.
6. Chen J, Wildman RP, Gu D, Kusek JW, Spruill M, Reynolds K, et al. Prevalence of decreased kidney function in Chinese adults aged 35 to 74 years. *Kidney Int*. 2005; **68**: 2837 – 2845.
7. Jafar TH, Schmid CH, Levey AS. Serum creatinine as marker of kidney function in South Asians: a study of reduced GFR in adults in Pakistan. *J Am Soc Nephrol*. 2005; **16**: 1413 – 1419.
8. Hsu CC, Hwang SJ, Wen CP, Chang HY, Chen T, Shiu RS, et al. High prevalence and low awareness of CKD in Taiwan: a study on the relationship between serum creatinine and awareness from a nationally representative survey. *Am J Kidney Dis*. 2006; **48**: 727 – 738.
9. Najafi I, Attari F, Islami F, Shakeri R, Malekzadeh F, Salahi R, et al. Renal function and risk factors of moderate to severe chronic kidney disease in Golestan Province, northeast of Iran. *PLoS One*. 2010; **5**: e14216.
10. Malekzadeh F, Marshall T, Pourshams A, Gharravi M, Aslani A, Nateghi A, et al. A pilot double-blind randomised placebo-controlled trial of the effects of fixed-dose combination therapy (polypill) on cardiovascular risk factors. *Int J Clin Pract*. 2010; **64**: 1220 – 1227.
11. Stewart JH, McCredie MR, Williams SM, Jager KJ, Trpeski L, McDonald SP. Trends in incidence of treated end-stage renal disease, overall and by primary renal disease, in persons aged 20-64 years in Europe, Canada and the Asia-Pacific region, 1998–2002. *Nephrology (Carlton)*. 2007; **12**: 520 – 527.
12. Wakai K, Nakai S, Kikuchi K, Iseki K, Miwa N, Masakane I, et al. Trends in incidence of end-stage renal disease in Japan, 1983–2000: age-adjusted and age-specific rates by gender and cause. *Nephrol Dial Transplant*. 2004; **19**: 2044 – 2052.
13. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: third National Health and Nutrition Examination Survey. *Am J Kidney Dis*. 2003; **41**: 1 – 12.
14. Kuo HW, Tsai SS, Tiao MM, Yang CY. Epidemiological features of CKD in Taiwan. *Am J Kidney Dis*. 2007; **49**: 46 – 55.
15. Sumaili EK, Krzesinski JM, Zinga CV, Cohen EP, Delanaye P, Mulyanganga SM, et al. Prevalence of chronic kidney disease in Kinshasa: results of a pilot study from the Democratic Republic of Congo. *Nephrol Dial Transplant*. 2009; **24**: 117 – 122.
16. Safarinejad MR. The epidemiology of adult chronic kidney disease in a population-based study in Iran: prevalence and associated risk factors. *J Nephrol*. 2009; **22**: 99 – 108.
17. Mahdavi-Mazdeh M, Saeed Hashemi Nazri S, Hajghasemi E, Nozari B, Zinat Nadia H, Mahdavi A. Screening for decreased renal function in taxi drivers in Tehran, Iran. *Ren Fail*. 2010; **32**: 62 – 68.
18. Hosseinpanah F, Kasraei F, Nassiri AA, Azizi F. High prevalence of chronic kidney disease in Iran: a large population-based study. *BMC Public Health*. 2009; **9**: 44.
19. Coresh J, Byrd-Holt D, Astor BC, Briggs JP, Eggers PW, Lacher DA, et al. Chronic kidney disease awareness, prevalence, and trends among U.S. adults, 1999 to 2000. *J Am Soc Nephrol*. 2005; **16**: 180 – 188.
20. Goldberg RB, Mellies MJ, Sacks FM, Moye LA, Howard BV, Howard WJ, et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the cholesterol and recurrent events (CARE) trial. The Care Investigators. *Circulation*. 1998; **98**: 2513 – 2519.
21. McKeown NM, Meigs JB, Liu S, Saltzman E, Wilson PW, Jacques PF. Carbohydrate nutrition, insulin resistance, and the prevalence of the metabolic syndrome in the Framingham Offspring Cohort. *Diabetes Care*. 2004; **27**: 538 – 546.
22. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal function: new insights into old concepts. *Clin Chem*. 1992; **38**: 1933 – 1953.