Screening for Asymptomatic Kidney Disease in High-Risk Population of Urmia, Iran

Ali Ghafari,[1] Elham Ahmadnezhad,[2] Nariman Sepehrvand,[3] Sanaz Hatami,[3] Saber Zafarshamspoor,[3] Barzan Ayubian,[3] Rebecca Erfani,[3] Gelare Jafari,[3] Farshid Fayyaz-Jahani[3]

[1]Nephro-Urology Research Center, Urmia University of Medical Sciences, Urmia, Iran
[2]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
[3]Students' Research Committee, Urmia University of Medical Sciences, Urmia, Iran

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Introduction. Screening programs for chronic kidney disease (CKD) are deemed to be cost effective only when they are limited to high-risk groups. We screened a sample of high-risk population of Urima, Iran.

Materials and Methods. As a pilot study for a national project, we enrolled 905 participants who had at least one risk factor for CKD (including hypertension, diabetes mellitus, or a family history of CKD). The study population was selected from among patients with Dm or hypertension and family members of those with CKD in Urima urban area and 2 randomly selected neighbor rural areas. Urine dipstick tests were done and blood sample was obtained to detect proteinuria and measure serum creatinine concentration, respectively.

Results. A total of 607 participants (67.1%) were enrolled from rural areas and 298 (32.9%) from the urban area. The mean serum creatinine level was 1.27 ± 0.60 mg/dL. A high serum creatinine level was demonstrated in 343 participants (37.9%), and 212 (23.4%) were demonstrated to have proteinuria. There was a significant correlation between serum creatinine level and urinary protein excretion (P = .001). There were no significant differences between rural and urban subgroups in terms of proteinuria (P = .42) and serum creatinine level (P = .08).

Conclusions. The prevalence of a high creatinine level (37.9%) is so high in the high-risk population of Urmia. Our most important goal of implementing this preliminary study was to assess probable limitations and problems of performing an extensive national screening program for CKD in the future.

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INTRODUCTION

Chronic kidney disease (CKD) is a major worldwide problem. Patients with the advanced stage of CKD, which is usually named end-stage renal disease, are consuming a huge proportion of the limited health resources of nations.[1] These patients are likely to represent the tip of the iceberg to the entire burden of CKD.[2]

Screening of CKD, in order to find patients in the early stages, is strongly recommended. There is a growing of evidence in support of the cost-effectiveness of CKD screening. One could screen the whole population to detect as many cases as possible. However, it was demonstrated that early detection of urinary protein, which can help to slow progression of CKD and decrease mortality,

was only cost effective when applied in high-risk groups.[3] Some major risk factors of CKD include hypertension, diabetes mellitus (DM), and a family history of CKD.[4] In India for example, DM and hypertension are responsible for 40% to 60% of all cases of CKD.[5]

The aim of this study was to screen CKD among high-risk individuals of Urmia, in the north-western region of Iran, in order to detect the CKD cases early and prevent subsequent huge financial and psychological burden of the disease.

MATERIALS AND METHODS

After obtaining the approval from the ethics board of Urmia University of Medical Sciences, the current cross-sectional study was performed in Urmia, the capital of West-Azerbaijan Province in the north-western region of Iran. Individuals older than 16 years old with DM, hypertension, or a positive family history of CKD were approached in this study. The target population included residents of both urban and rural areas of Urmia. We enrolled high-risk groups from the urban area by referring to the clinic of CKD care, the Clinic of Kidney Transplant Recipients in Imam-Khomeini Hospital, and the Hemodialysis Center in Taleqani Hospital to approach to the family members of patients with kidney disease. We also enrolled the members of Urmia Association for Supporting Diabetic patients by an announcement. Among different rural areas around Urmia, Kahriz region in the north of Urmia and Anhar region in the west were selected randomly. All the mentioned high-risk populations from Kahriz and Anhar regions were included in the study by healthcare staff responsible for health service facilities in the villages. Each participant signed an informed consent for participation. Diabetic or hypertensive patients with nephropathy and those who did not consent for participation were excluded from the study population.

We collected data on the information about personal characteristics, including as age, sex, height, and weight, smoking, drug history, history for DM, hypertension, kidney disease, familial history for kidney disease, laboratory findings (urinalysis and serum creatinine). Systolic and diastolic Blood pressures were measured only in one occasion. A urine dipstick (Medi-Test Combi 9- Macherey Nagel, Duren, Germany) was performed for each patient. Two milliliters of blood sample were collected from each patient through venipuncture to investigate for serum creatinine level. A high serum creatinine level was considered 1.5 mg/dL or higher in men and 1.3 mg/dL or higher in women. All individuals with a positive test result for kidney dysfunction or damage in the screening were referred to nephrologists, but they were not followed up.

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, Ill, USA). The independent *t* test was used to compare quantitative variables, and the chi square test to compare proportions between groups. *P* values lower than .05 were considered significant. Continuous variables were presented as mean ± standard deviation.

RESULTS

Nine hundred and twenty individuals without an established diagnosis of CKD were included in the study, of whom 15 were excluded because of incomplete data, and 905 subjects were included in the analyses. They were 587 women (64.9%) and 318 men (35.1%). The study population consisted of 607 participants from rural areas (67.1%), and 298 from urban areas of Urmia (32.9%). The mean age of the participants was 52.5 ± 15.1 years (95% confidence interval [CI], 51.6 to 53.5; range, 13 to 90 years).

The mean body mass index (BMI) was 28.51 ± 5.59 kg/m^2 (95% CI, 28.15 to 28.88). One hundred and ninety-seven participants (21.8%) were smokers. The mean systolic blood pressure was 132.00 ± 20.44 mm Hg (95% CI, 130.66 to 133.33), and the mean diastolic blood pressure was 77.00 ± 12.23 mm Hg (95% CI, 76.90 to 77.88). Of 905 participants, 201 (22.2%) were only diabetic, 150 (16.6%) were only hypertensive, and 101 (11.2%) only had a positive familial history for CKD. Concurrent DM and hypertension were present in 201 participants (22.2%), 104 (11.5%) were diabetic patients who had a positive familial history of CKD, 118 (13%) were hypertensive patients who had a positive familial history of CKD, and 30 (3.3%) were diabetic and hypertensive patients with a positive familial history of CKD (Table). The rural and urban subgroups were different in age (mean, 54.2 ± 14.3 years versus 49.1 ± 15.9 years, respectively; $P < .001$), sex distribution (women,

Characteristics of Screened Participants at Risk of Chronic Kidney Disease*

Parameter	Population at Risk							
	DM	HTN	FH	DM + HTN	DM + FH	HTN + FH	DM + HTN + FH	All
Patients (%)	201 (22.2)	150 (16.6)	101 (11.2)	201 (22.2)	104 (11.5)	118 (13.0)	30 (3.3)	905 (100)
Mean age, y	55.0 ± 12.9	57.7 ± 12.2	34.7 ± 12.6	54.8 ± 14.1	53.6 ± 14.3	55.5 ± 13.6	41.2 ± 16.4	52.5 ± 15.1
Sex								
Male	88	35	45	31	37	43	7	318
Female	113	115	56	138	67	75	23	587
BMI, kg/m^2	27.1 ± 5.5	30.6 ± 5.2	26.2 ± 5.5	28.5 ± 5.2	28.6 ± 5.4	29.2 ± 5.3	31.4 ± 6.6	28.5 ± 5.6
SBP, mmHg	126.6 ± 18.5	135.6 ± 21.0	118.8 ± 13.4	138.8 ± 21.6	126.3 ± 14.7	138.1 ± 21.1	144.1 ± 19.9	132.0 ± 20.4
DBP, mm Hg	75.7 ± 11.1	77.3 ± 13.2	72.5 ± 11.3	78.8 ± 13.1	75.6 ± 10.5	81.1 ± 12.1	77.1 ± 11.5	77.0 ± 12.2
Smoking	42 (20.9)	28 (18.6)	29 (28.7)	47 (23.3)	23 (22.1)	25 (21.2)	3 (10.0)	197 (21.8)
Mean SC, mg/dL	1.10 ± 0.54	1.50 ± 0.56	0.83 ± 0.41	1.46 ± 0.58	1.18 ± 0.52	1.36 ± 0.65	1.44 ± 0.70	1.27 ± 0.60
Proteinuria	43 (21.3)	46 (30.7)	11 (11.9)	55 (27.4)	19 (18.4)	29 (24.5)	9 (30.0)	212 (23.4)

*Values in parentheses are percents. DM indicates diabetes mellitus; HTN, hypertension; FH, family history of chronic kidney disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; and SC, serum creatinine.

70.1% versus 54.0%, respectively; $P < .001$), and BMI (mean, 28.97 ± 5.59 kg/m^2 versus 27.59 ± 5.47 kg/m^2, respectively; $P < .001$).

The mean serum creatinine level was 1.27 ± 0.60 mg/dL (95% CI, 1.24 to 1.31), and 343 participants (37.9%) demonstrated to have a high serum creatinine level. Also, 212 participants (23.4%) demonstrated to have proteinuria in their urine dipstick study. There was a significant correlation between serum creatinine level and urinary protein excretion ($P = .001$). This correlation also existed when the analysis applied for each residential subgroup. Considering serum creatinine level as a standard for diagnosing CKD proteinuria had a sensitivity, specificity, positive predictive value, and negative predictive value of 44%, 89%, 71%, and 72%, respectively, for prediction of a high serum creatinine level.

There were no significant differences in the prevalence of proteinuria ($P = .44$) and high serum creatinine level ($P = .13$) between women and men. Neither was any differences between the two residential groups (rural and urban groups) in the prevalence of proteinuria, which was seen in 144 participants (23.7%) from the rural areas and 68 (22.8%) from the urban area ($P = .42$). The mean serum creatinine level was 1.30 ± 0.59 mg/dL and 1.22 ± 0.62 mg/dL in participants from the rural and urban areas, respectively ($P = .08$). Categorizing participants into 2 groups with high versus low creatinine levels, 311 (51.2%) in the rural subgroup and 123 (41.2%) in urban subgroup demonstrated to have a high creatinine level ($P = .003$). However, there was no significant difference in the frequency of high creatinine level between the two residential subgroups when data were adjusted for age, sex, and BMI.

Smoking did not have a relation with proteinuria or high serum creatinine level. Neither was a relationship between BMI and serum creatinine level, except for the diabetics subgroup ($P < .001$).

DISCUSSION

According to the study of Nafar and colleagues in 2004, Over 700 000 people were estimated to have CKD in Iran. The prevalence rate of CKD was estimated to be 1083 and its incidence rate was 173.5 per year per 100 000 population. Chronic kidney disease was responsible for 1 145 654 disability-adjusted life years.[6] Delayed recognition and treatment of CKD may predispose patients to adverse outcomes.[7] Some of the more important negative outcomes include more rapid onset of end-stage renal disease, progression of comorbid conditions such as anemia and cardiovascular disease, suboptimal vascular access at initiation of dialysis, increased use of centre-based hemodialysis, increased hospitalization, increased cost, and worse survival.[8] Early detection of disease via performing screening programs is widely recommended.[9]

In this study, we utilized urinary protein excretion and serum creatinine level for screening of the population at risk for CKD. The study by Iseki in the Okinawa region of Japan demonstrated that proteinuria and high serum creatinine level are two valuable prognostic factors for end-stage renal disease.[10] Our study demonstrated a high prevalence of high serum creatinine level as an

indicator of CKD among the high-risk populations of Urmia, including patients with DM, hypertension, and also apparently healthy people with a family history of CKD. We showed a specificity of 89% for urine dipstick study of proteinuria to predict a high serum creatinine level as the standard. This means that dipstick may be an appropriate test for diagnosing kidney damage in asymptomatic individuals and can suggest that with a negative urinary test tape study, there is no need for further evaluation for a while; however, there is much less consensus on the time recommended to be considered for the next assessment. We used serum creatinine as the base to diagnose CKD; however, it would be better to utilize glomerular filtration rate (GFR) formulas to measure GFR for this aim, because an overtly high serum creatinine level (if measured) is more likely to draw the physician's attention compared to a diminished GFR with a "normal appearing" creatinine level, especially in the elderly.[11]

Several studies have been performed to screen for CKD among the Iranian general population. Hosseinpanah and coworkers, in a large population-based study on 10 063 people, found an overall prevalence of 18.9% for CKD in Tehran.[12] Mahdavi-Mazdeh and colleagues, despite using similar equation for determining CKD cases (the Modification of Diet in Renal Disease equation), did not apply the term "prevalence of CKD," and reported the prevalence of an estimated GFR less than 60 mL/min/1.73 m^2 among taxi drivers of Tehran to be 6.5%.[13] The criteria for determining CKD cases in our study (serum creatinine level and spot urine proteinuria) is relatively less specific than the criteria in the two abovementioned studies (calculating GFR). The prevalence of a high serum creatinine level in our study (37.9%) is higher than that in these two other Iranian studies. The most important disparity between our study and these studies was the population characteristics, which, in our study, is limited to the high risk groups, while in the studies of Hosseinpanah and colleagues and Mahdavi-Mazdeh and colleagues, screening was performed among the general population.[12,13]

In the study of Iseki, age and obesity had no influence on the incidence of end-stage renal disease,[10] whereas in our study, there was a correlation between BMI and serum creatinine level in the diabetic population. On the other hand, the frequency of high creatinine level was associated with increasing age and BMI in the participants from the rural areas of Urmia, compared with the urban residents.

More than 70% of our participants in the rural areas were women. This was a source of selection bias because our screening team referred to villages in the morning (working time of healthcare centers), and at this time of the day, most of men in the rural areas were at work, and therefore, they were not present in the healthcare centers. This raised a problem in our interpretation of the results; the sample population from rural areas was not a representative of the high-risk group of that area. Previous studies proposed men to be affected more likely by CKD or end-stage renal disease compared with women,[7,10] but in the current study, there were no significant differences in the frequency of proteinuria and high serum creatinine level between the two sex groups.

CONCLUSIONS

The most important goal of implementing this preliminary study was to perceive the probable limitations and problems of performing an extensive national screening program for CKD. The followings not only are the limitations of current pilot study, but also are the most important results of it: (1) This study did not include any follow-up of the subjects, and so no data is available regarding the outcome of disease. (2) Data regarding the treatment regimens for the therapy of DM or hypertension in diabetic and hypertensive patients were not completely available. We suggest that in the future projects, the screening team members be trained very well about the importance of filling all inquired data. (3) In this study we used volunteer researchers for our screening team, but this experience determined that a screening project needs more formal and institutional involvement of healthcare system. Although there may be some resistance against the active involvement of healthcare workers in such programs, this involvement is essential to performing an extensive screening program properly. (4) We had some limitations regarding our applied criteria for the diagnosis of CKD (high serum creatinine level and proteinuria in dipstick study), and it could be better to use other standard methods of determining CKD, such as calculating GFR. However, some doubts remain about the

feasibility of using GFR formulas for determining CKD (especially by the healthcare workers) in the future screening programs. (5) As mentioned above, most of participants in the rural areas were women and men rarely consented to participate in the study, because the screening team referred to villages in the morning, and this was the time men are at work in rural areas. Therefore, any future screening program should take some actions in order to solve this problem. Finally, because of the differences in the prevalence and incidence of CKD in our region compared to other regions of Iran,[14] our results may not be applicable in other regions of Iran or other countries. More educational programs about the increasing risk of CKD in the population, especially among high-risk groups, should be planned.

CONFLICT OF INTEREST

None declared.

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Correspondence to:
Nariman Sepehrvand, MD
Deputy for Research Affairs, Urmia University of Medical Sciences, Resalat Ave, Djahad Sq, Urmia, Iran
Tel: +98 441 223 1930
Fax: +98 441 223 1930
E-mail: nariman256@gmail.com

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