Self-Assessment Symptoms and Risk Factors for Chronic Kidney Disease Screening in Primary Care

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ABSTRACT

Chronic kidney disease (CKD) is a serious disease that is commonly undetected and for which screening is advocated. Risk factors and symptoms are associated with the prevalence of CKD. To identify symptoms and risk factors that should be used for screening CKD in primary care. Literature review had been performed from 1960-February 2007 to review symptoms and risk factors of the CKD. Only variables that were easy to assess without any laboratory tests or other clinical measurements requiring special skills were selected. The interview was performed in general population volunteers of 1,208 Thai, aged 20-88 years, to collect kidney disease-related symptoms and risk factors. Subsequently, blood samples were collected for serum creatinine test and urinalysis was also carried out. This study found glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 in 22.5 percent and proteinuria in 14.1 percent. The people with GFR < 60 ml/min/1.73 m^2 were significantly older, had a history of stone, diabetes, hypertension, female, hematuria, chronic foaming urine, frequent straining when urinating, frequent dribbling at the end of urination and renal colic ($P < 0.05$). Predictors of proteinuria were age, smoking, systolic blood pressure, stone, diabetes, hypertension, daily use of NSAIDs ≥ 1 year, female, hematuria, chronic foaming urine, frequent straining when urinating, frequent hesitating when urinating, frequent dribbling at the end of urination, frequent nocturia and edema ($P < 0.05$). Symptoms and risk factors of CKD can be used as a self-assessment method to identify people with high risk of CKD.

Key words: Chronic kidney disease, Chronic renal disease, Screening, Primary care unit, Symptom, Risk factor

INTRODUCTION

Chronic kidney disease (CKD) is a growing public health problem. The major outcomes of CKD are loss of kidney function, leading to complications and kidney failure, and development of cardiovascular disease (K/DOQI, 2002; Go et al., 2004). Adverse outcomes of CKD can often be prevented or delayed through early detection and treatment. Kidney Disease Outcome Quality Initiative (K/DOQI) guidelines 2002 recommend that screening tests for CKD are tests for proteinuria and estimation of GFR from serum creatinine (SCr) by prediction equations (K/DOQI, 2002). To identify people with CKD, at least SCr is needed, but it has been shown that screening for CKD in general population is not cost-effective. Proteinuria is most often screened by urinary dipstick test which is limited because of the low sensitivity and specificity and should be confirmed by a quantitative measurement for establishing diagnosis. Therefore, dipstick urinalysis has imperfect accuracy in the diagnosis of persistent proteinuria. Furthermore, there is non cost-effectiveness in screening for CKD by dipstick test for general population ($282,818 per quality-adjusted life-year) due to prevalence of CKD is very low. Cost-effectiveness ratios are far more favorable in persons with risk factors for CKD (hypertension, diabetes and older age), in which the prevalence of CKD is greater (Boulware et al., 2003).

Clinical practice guidelines for the treatment of CKD recommend regular screening of individuals with risk factors for CKD (K/DOQI, 2002). These recommendations focus on risk factors of CKD. Clinical presentations are specific for types of kidney disease (Massy and Glassock, 2001; K/DOQI, 2002). There are (1) nephritic and nephrotic syndromes (2) kidney disease with urinary tract symptoms (3) asymptomatic urinalysis abnormalities and (4) high blood pressure (BP) due to kidney disease. Symptoms based on clinical presentation of kidney disease were included to study. Our aim in the present study was to identify symptoms and risk factors that should be used for screening for CKD in primary care.

MATERIALS AND METHODS

Between February – April 2008, a descriptive study was done in Pone-Ngam primary care unit, Boontharig Hospital, Ubon Ratchathani Province. Most of the participants were rural dwellers of low-income social class. The face-to-face interview by trained interviewers was performed in general population samples of 1,208 Thai, aged 20-88 years, not known to have CKD, to collect kidney disease-related symptoms and risk factors or independent variables. Subsequently, they underwent blood test for SCr and urinalysis (dipstick test) for proteinuria to be used as the dependent variables. The study was approved by the Human Research Ethical Committee of the Faculty of Medicine, Khon Kaen University, Thailand. Written informed consent for each participant was obtained.

Statistical Analysis

Data are presented as mean±SD for continuous variables and as proportions for categorical variables. A Mann-Whitney test was applied for a comparison of group means, and a Chi-Square test was applied for proportions. Statistical analysis was performed using SPSS software version 15 for Window. All probabilities were two-tailed and p value less than 0.05 was considered statistically significant.

CKD was defined as a positive urine dipstick test to detect proteinuria (1+ or more result on a colorimetric urine dipstick test for gross proteinuria) or GFR < 60 ml/min/1.73 m^2 (K/DOQI, 2002). Estimated GFR was calculated using the abbreviated Modification of Diet in Renal Disease Study (MDRD) equation: GFR (ml/min/1.73 m^2) = 186.3 x $(SCr)^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 for women).

Literature review was performed to review symptoms and risk factors specific to CKD. Only symptoms and risk factors that were easy to assess without any tests or other clinical measurements requiring special skills were selected. Questions were on symptoms commonly considered related to kidney disease. Selected symptoms based on clinical presentation of kidney disease consist of (1) nephritic and nephrotic syndromes (edema, high BP, gross hematuria) (2) kidney disease with urinary tract symptoms (dysuria and frequency, hesitating, straining, dribbling, nocturia, renal colic, frank pain) (3) asymptomatic urinalysis abnormalities (chronic foaming urine representing indicator of proteinuria) and (4) high BP due to kidney disease (Massy and Glassock, 2001; K/DOQI, 2002). The risk factors items included diabetes, hypertension, gout, nephrolithiasis or history of small stones passed in the urine, body mass index (BMI), male sex, age, smoking, and history of non-steroidal antiinflammatory drugs (NSAIDs) and paracetamol use .

An electronic BP measurement was used to measure BP. All BP measurements were taken after at least a 5-minute period in the sitting position. Body weight was measured by electronic scale while the subjects wore light clothing and no shoes. Weight was recorded in the pattern of one decimal point. Height was assessed to the nearest 0.5 cm, using a wall-mounted stadiometer on subject standing upright and not wearing shoes, with their arms to the side, ankles or knees together, heels together, and head in the horizontal Frankfurt plane. BMI was calculated as weight in kilogram divided by the square of the height in metre. Detailed informations about average number of cigarettes/day, years, and pack-years were collected (Pinto-Sietsma et al., 2000). The amount of tobacco consumed over time was defined as pack-years (the mean number of daily cigarettes smoked divided by 20 and multiplied by the number of smoking years) (Orth et al., 1998). History of NSAIDs and paracetamol use was asked about the average frequency of their analgesic drug use (days per week, month, or year). Average intake was categorized as light (0 to 104 pills per year, or 0 to 2 pills per week), moderate (105 to 365 pills per years, or more than 2 pills per week to 1 pill per day) or heavy (366 or more pills per year, or more than 1 pill per day).

RESULTS

Of the participants, 1,208 completed blood test for SCr and urinalysis, which resulted in the identification of 272 subjects with GFR < 60 ml/min/1.73 m^2 and 171 subjects with proteinuria. The percentage of subjects with missing information concerning one of the symptoms or risk factors did not exceed 1.4% per item. Most of them were female (817 cases, 67.6%). Mean age was 49.24 ± 13.27 years. The prevalence of diabetes mellitus was 5.7%. Hypertension was diagnosed in 13.2%. Known stone was 8.3%.

The people with GFR < 60 ml/min/1.73 m^2 were significantly older, had a history of stone, diabetes, hypertension, female, hematuria, chronic foaming urine, frequent straining when urinating, frequent dribbling at the end of urination and renal colic (Tables 1-3). Statistically significant independent predictors of proteinuria were age, smoking pack-year, systolic BP, stone, diabetes, hypertension, daily use of NSAIDs ≥ 1 year, female, hematuria, chronic foaming urine, frequent straining when urinating, frequent hesitating when urinating, frequent dribbling at the end of urination, frequent nocturia and edema (Tables 4-6).

Table 1. Comparison of symptoms between the population with and without GFR < 60 ml/min/1.73 m^2.

	GFR ≥ 60 ml/min/1.73 m^2 (%)	**GFR < 60 ml/min/1.73 m^2 (%)**	**p-value**	**Crude odd ratios**
Chronic hematuria	6.84	10.66	0.037	1.63 (1.00 – 2.64)
Chronic foaming urine	15.71	27.57	< 0.001	2.04 (1.47 – 2.85)
Frequent dysuria	11.98	16.18	0.069	1.42 (0.95 – 2.10)
Frequent straining when urinating	6.62	10.66	0.026	1.68 (1.03 – 2.74)
Frequent hesitating when urinating	7.47	10.66	0.092	1.48 (0.91 – 2.38)
Frequent dribbling at the end of urination	16.45	21.77	0.043	1.41 (1.00-2.00)
Frequent nocturia	9.63	8.09	0.442	0.83 (0.49-1.38)
Edema	7.26	6.25	0.565	0.85 (0.47 – 1.52)
Frank pain	14.32	13.60	0.766	0.94 (0.62 – 1.42)
Renal colic	23.74	32.35	0.004	1.54 (1.13- 2.09)

Table 2. Comparison of risk factors between the population with and without GFR < 60 ml/min/1.73 m^2.

	GFR ≥ 60 ml/ min/1.73 m^2 (%)	**GFR < 60 ml/ min/1.73 m^2 (%)**	**p-value**	**Crude odd ratios**
Stone	7.37	11.76	0.021	1.68 (1.05 – 2.66)
Diabetes	3.42	13.60	< 0.001	4.45 (2.64-7.50)
Hypertension	9.84	25.37	< 0.001	3.11 (2.17-4.47)
Gout	1.71	2.21	0.607	1.30 (0.45 – 3.57)
Daily use of NSAIDs ≥ 1 year	2.46	2.57	0.916	1.05 (0.40-2.60)
Daily use of paracetamol ≥ 1 year	3.52	2.94	0.639	0.83 (0.35-1.90)
Female	66.13	72.79	0.039	1.37 (1.01-1.87)

Table 3. Comparison of risk factors (continuous variables) between the population with and without GFR < 60 ml/min/1.73 m^2.

	GFR ≥ 60 ml/min/1.73 m^2 (Mean ± SD)	**GFR < 60 ml/min/1.73 m^2 (Mean ± SD)**	**p-value**
Age			
46.95 ± 12.45	56.91 ± 13.16	< 0.001	
Smoking Pack-year	4.51 ± 10.70	4.32 ± 11.37	0.102
Body mass index	24.53 ± 4.12	24.28 ± 3.71	0.638
Systolic blood pressure	115.92 ± 16.96	118.28 ± 18.32	0.089
Diastolic blood pressure	74.40 ± 10.52	73.87 ± 10.31	0.411

Table 4. Comparison of symptoms between the population with and without proteinuria.

	Without proteinuria (%)	With proteinuria (%)	p-value	Crude odd ratios
Chronic hematuria	6.65	14.04	0.001	2.29 (1.35-3.86)
Chronic foaming urine	14.85	39.77	< 0.001	3.79 (2.63 -5.46)
Frequent dysuria	12.36	16.37	0.147	1.39 (0.87 – 2.21)
Frequent straining when urinating	6.75	12.28	0.011	1.93 (1.11 – 3.33)
Frequent hesitating when urinating	7.23	14.04	0.003	2.09 (1.24 – 3.51)
Frequent dribbling at the end of urination	16.01	27.65	< 0.001	2.00 (1.35-2.96)
Frequent nocturia	7.82	18.13	< 0.001	2.61 (1.62-4.19)
Edema	5.88	14.04	< 0.001	2.61 (1.53 – 4.44)
Frank pain	14.08	14.62	0.851	1.04 (0.64 – 1.69)
Renal colic	24.71	31.58	0.057	1.41 (0.97 – 2.03)

Table 5. Comparison of risk factors between the population with and without proteinuria.

	Without proteinuria (%)	With proteinuria (%)	p-value	Crude odd ratios
Stone	7.04	16.37	< 0.001	2.59 (1.57-4.23)
Diabetes	3.95	16.37	< 0.001	4.76 (2.76-8.17)
Hypertension	11.49	24.56	< 0.001	2.51 (1.65-3.80)
Gout	1.54	3.51	0.112	2.32 (0.80-6.42)
Smoking	16.10	20.47	0.157	1.34 (0.87 – 2.05)
Daily use of NSAIDs ≥ 1 year	2.03	5.29	0.028	2.70 (1.13-6.34)
Daily use of				
paracetamol ≥ 1 year	3.66	1.75	0.201	0.47 (0.11-1.61)
Female	69.24	57.89	0.003	0.61 (0.43-0.86)

* Fisher's Exact Test

Table 6. Comparison of risk factors (continuous variables) between the population with and without proteinuria.

	Without proteinuria (Mean ± SD)	With proteinuria (Mean ± SD)	p-value
Age	47.85 ± 12.85	57.34 ± 12.93	< 0.001
Smoking Pack-year	3.95 ± 9.80	7.56 ± 15.45	0.006
Body mass index	24.55 ± 4.02	24.00 ± 4.09	0.070
Systolic blood pressure	115.77 ± 16.82	120.53 ± 19.53	0.005
Diastolic blood pressure	74.21 ± 10.36	74.72 ± 11.18	0.312

DISCUSSION AND CONCLUSION

In the present study, we demonstrate that the specific symptoms of kidney disease, such as frequent hematuria, edema, nocturia or chronic foaming urine are associated with GFR < 60 ml/min/1.73 m^2 or proteinuria. When present, hematuria should be regarded as a sign of disease originating in the kidneys, of lesions present anywhere along the urinary tract from the renal pelvis to the distal urethra. Hippocrates noted that foaming urine was associated with kidney disease. Diskin et al., (2000) investigated whether the changes in surface tension that cause bubble formation in spot urine samples may represent indicator of 24-h proteinuria. The results of all tests were correlated with protein concentrations in 24-h urine collections. Edema may occur if the kidneys are unable to excrete excess water and sodium from the body. Edema may also develop from a kidney disorder that causes the loss of large amounts of protein in the urine (nephrotic syndrome). In the early stages of many kidney disorders, a person may need to urinate frequently during the night (nocturia). Nocturia may occur as the consequence of an edema-forming state such as nephrotic syndrome. The supine position during sleep promotes reabsorption of edema with subsequent urine production. Frequent urination of very small amounts at night may result when the flow of urine into and through the urethra is obstructed and urine backs up in the bladder; an enlarged prostate is the most common cause of obstruction in older men. We also found that the presence of symptoms that indicate a partially-obstructed urethra, enlarged prostate or stone, such as frequent straining when urinating, frequent hesitating when urinating, frequent dribbling at the end of urination or renal colic, also increase the risk for GFR < 60 ml/min/1.73 m^2 or proteinuria (Massy and Glassock, 2001; K/DOQI, 2002).

In the present study, the authors found the association between the classical risk factors of age, diabetes, hypertension and stone with GFR < 60 ml/min/1.73 m^2 or proteinuria. Many epidemiological studies have reported the same factors to be correlated with CKD. It has been widely accepted that the GFR declines with age. The prevalence of decreased GFR is higher in the elderly. Approximately 14.9 million (74.5 %) individuals ≥70 years of age have decreased GFR (K/DOQI, 2002, Fox et al., 2004). Diabetes and hypertension are key risk factors for the development of CKD (Hoy et al., 1998; Ramirez et al., 2002; Fox et al., 2004).

Diabetic kidney disease affects 20 to 30 percent of patients with diabetes (Thorp, 2005). Elevated BP is an important modifiable risk factor for progressive CKD, regardless of the initial cause of kidney injury. Evidence from clinical trials shows that BP reduction reduces the rate of loss of renal function and progression to renal failure and this information has been incorporated into widely-disseminated clinical practice guidelines. These studies have demonstrated a strong and graded association between BP reduction and reduction in rate of decline in GFR that persists to BP levels of 130/80 mmHg, and this threshold has been adopted for management of hypertensive patients with CKD (McClellan, 2005). Stone disease is often complicated with some events which may damage kidney tissue, such as obstruction and infection, due to the passage of calculi along the urinary tract. The above events are important risk factors for the development of CKD (Marangella et al., 1990).

In conclusion, this study reported that specific symptoms and risk factors of CKD are associated with GFR < 60 ml/min/1.73 m^2 or proteinuria. Therefore, easy-to-assess symptom and risk factors should be used for CKD screening in general population. These could also be used in symptom-awareness campaigns. It may also prompt individuals and health care professionals to perform simple tests to assess variable such as GFR or proteinuria (Kannel et al., 1976).

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