Original Article

Prevalence of Chronic Kidney Disease among Family Members of Hemodialysis Patients at the Bhumirajanagarindra Kidney Institute

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Background: The prevalence of chronic kidney disease (CKD) is estimated to be 8% to 16% worldwide and 8.9% in the general population of Thailand. There is minimal information about prevalence of CKD among family members of end stage renal disease (ESRD) patients.

Objective: To investigate the prevalence of CKD among first-degree relatives of dialysis patients in Thailand.

Materials and Methods: The present observational study was conducted in first degree relatives of dialysis patients at the Bhumirajanagarindra Kidney Institute. Participants aged between 18 and 60 years old were enrolled for CKD screening. CKD was defined by the KDIGO criteria.

Results: One hundred seventy-nine participants were enrolled. The average age was 45.9±9.9 years and the average eGFR was 103.3±13 ml/minute/1.73 m^2. The median urine albumin creatinine ratio (UACR) was 7 (2 to 985) mg/g Cr. The prevalence of combined CKD stages 1 and 2 was 6.2%. Factors associated with CKD were diabetes, history of using non-steroidal anti-inflammatory drugs (NSAIDs), and history of using angiotensin-converting enzyme (ACEI)/angiotensin II receptor blocker (ARB).

Conclusion: The prevalence of CKD among the first-degree relatives of dialysis patients was 6.2%. Early screening of early CKD and prevention program including education should be introduced to this group of people.

Keywords: Prevalence, Chronic kidney disease, Urine albumin creatinine ratio, Hemodialysis, First degree relative

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Chronic kidney disease (CKD) is a growing health problem worldwide. The prevalence of CKD is estimated to be 8% to 16%[1]. In Thailand, the overall prevalence of CKD stages 1 to 2 is 8.9%[2]. CKD causes multiple complications and consequences. It is an independent risk factor for cardiovascular disease and overall morbidity[3]. Moreover, cost of CKD treatment including renal replacement therapy (RRT) is high. It contributes to a sizeable proportion of health-care expense[4,5].

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Several studies have shown the benefit of early detection and treatment of CKD in slowing renal disease progression and decreasing adverse outcomes. However, universal screening for CKD in general population is not cost-effective and not recommended[6,7]. The screening program is usually reserved for those who are at risk of developing CKD. These risk factors include old age, diabetes, hypertension, smoking, cardiovascular diseases, and family history of CKD[8]. It has been observed that family members of end stage renal disease (ESRD) patients have high prevalence of CKD[9-12]. This could have been due to genetic factors or common environmental factors related to their family aggregation[12-14]. In the present study, the authors analyzed the prevalence of CKD among family members of ESRD patients in Thailand.

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Materials and Methods

The authors conducted an observational study at the Bhumirajanagarindra Kidney Institute, Bangkok between January and September 2016. The study protocol was approved by the Institutional Ethical Committee.

Patients

Subjects were enrolled if they met the inclusion criteria which was 1) age 18 to 60 years of either sex, 2) first-degree relatives of the dialysis patients at Bhumirajanagarindra Kidney Institute, Bangkok. The exclusion criteria were 1) age older than 60 years, 2) the cause of ESRD in their respective relatives was genetic disease such as alport syndrome or autosomal polycystic kidney disease (ADPKD), 3) cancer, 4) pregnancy, 5) HIV infection, 6) chronic pyelonephritis, or 7) history of use of nephrotoxic drugs. Written informed consent was obtained prior to enrollment.

Methods

Clinical data were obtained from the subjects. We included subjects from suggestion by the dialysis patients. Body weight and height were measured with a digital scale and linear height scale, respectively. Body mass index (BMI) was calculated. Blood pressure was measured at rest with digital sphygmomanometer (Mindray VS-800, Shenzhen Mindray Bio-Medical Electronics Co., Ltd., Germany). Blood pressure higher than 140/90 mmHg was defined as hypertension[15].

Laboratory analysis

During the first visit, venous blood was drawn for measurement of creatinine (Cr), urine for urine albumin creatinine ratio (UACR) and urine was collected in the morning. Cr was assayed with enzymatic method[16,17]. Estimated glomerular filtration rate (eGFR) was calculated with CKD-EPI equation[18]. CKD staging was based on KDIGO criteria: stage 1, CKD was defined as eGFR greater than 90 ml/minute/1.73 m^2 body surface area (BSA) and UACR greater than 30 mg/g Cr; and stage 2, CKD as eGFR between 60 and 89 ml/minute/1.73 m^2 BSA, and UACR greater than 30 mg/g Cr. These abnormalities must have persisted for more than three months.

Outcome of the study

Prevalence of CKD in family members of dialysis patients and risk factors for CKD.

Statistical analysis

The sample size calculation for estimating the infinite population proportion. The present study used prevalence of CKD from previous study. The prevalence of CKD in Spouses and Relatives of Hemodialysis Patients was found prevalence 16%. The delta and alpha errors were set at 0.05[19,20]. Sample size from calculation was 280 cases including 5% of estimated errors in the sample size. Data were presented as mean ± standard deviation (SD) for continuous variables, and number and/or percentage (%) for categorical variables. Some data were presented as median (range) for non-continuous variables. Statistical difference was analyzed with Chi-square, Fisher's exact test or independent t-test where appropriate. A p-value of less than or equal to 0.05 was considered statistically significant. The SPSS 17 program was used for statistical analyses.

Results

Patient characteristics

During the eight months of study, 179 subjects (71.6%) were enrolled from 250 families. The mean age was 45.9±9.9 years, 28% were male and 72.1% female. The most frequent relationship with index dialysis patients were offspring (son or daughter of dialysis patient). Common comorbid diseases included hypertension (11.7%) and diabetes (7.8%). Most of hypertensive subject received angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blockade (ARB) to control blood pressure. The subjects in the present study had history of using non-steroidal anti-inflammatory drugs (NSAIDs) (44.1%) and history of using herbal (27.4%).

The mean of BMI was 24.1 kg/m^2. The systolic and diastolic blood pressure were 120±19.9 and 73±13.7 mmHg, respectively. The serum Cr was 0.72±0.16 mg/dl, and the eGFR was 103±13 ml/minute/1.73 m^2 BSA. The blood sugar and low-density lipoprotein cholesterol (LDL) were 103±30 mg/dl and 129.4±34.2 mg/dl, respectively. UACR median was 7 (2 to 985) mg/g Cr (Table 1).

Among 179 subjects enrolled, 17 subjects (9.5%) showed abnormal initial laboratory tests such as eGFR of less than 60 cc/minute/1.73 m^2 BSA in one subject and high UACR of more than 30 mg/g Cr in 16 subjects. Three months thereafter, when the second screening test was done, 11 subjects (6.2%) showed persistent laboratory abnormality as high UACR, greater than 30 mg/g Cr in all (Figure 1), compatible with a diagnosis of CKD according to KDIGO's criteria[21].

Table 1. Demographic characteristics of 179 subjects

	n (%)
Number	179 (100)
Relationship with dialysis patient	
Parent	2 (1.1)
Offspring (son/daughter)	157 (87.7)
Brother/sister	20 (11.0)
Age (years), Mean±SD	45.9±9.9
Sex	
Male	50 (27.9)
Female	129 (72.1)
Diabetes[@]	14 (7.8)
Hypertension[#]	21 (11.7)
Kidney disease	1 (0.6)
Heart disease[$]	2 (1.1)
Alcohol consumption	59 (33.0)
Smoking	28 (15.6)
Regular exercise	96 (53.6)
History of using ACEI/ARB	21 (11.7)
History of using NSAIDs	79 (44.1)
History of using herbal[†]	49 (27.4)
BMI (kg/m^2), Mean±SD	24.14±5
Body weight (kg), Mean±SD	63.12±15
Systolic blood pressure (mmHg), Mean±SD	120.4±20
Diastolic blood pressure (mmHg), Mean±SD	73.9±13.7
Serum creatinine (mg/dl), Mean±SD	0.72±0.1
eGFR (ml/minute/1.73 m^2 BSA), Mean±SD	103±13
FBS (mg/dl), Mean±SD	103±30
LDL (mg/dl), Mean±SD	129.4±34.2
UACR (mg/g Cr)	
Mean±SD	21±78
Median (range)	7 (2 to 985)

SD=standard deviation; ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blockade; NSAIDs=non-steroidal anti-inflammatory drugs; BMI=body mass index; eGFR= estimated glomerular filtration rate; FBS=fasting blood glucose; LDL=low density lipoprotein cholesterol; UACR=urine albumin creatinine ratio

[@] Diabetes: FBS>126 or HbA1c>7, [#] Hypertension: blood pressure >140/90 mmHg, [$] Heart disease: acute and chronic coronary heart disease and arrhythmia disease, [†] Herbal: include Thai and Chinese herb

Among these 11 CKD subjects (Table 2), the systolic and diastolic blood pressure were significantly higher than those without CKD (138.2±9.9 versus 119.2±19.9 mmHg, p=0.002, and 83.0±9.0 versus 73.3±13.8 mmHg, p=0.0023, respectively). The BMI was 26.5±5.1 kg/m², the serum Cr 0.67±0.12 mg/dl, and the eGFR 104±16 ml/minute/1.73 m² BSA. Expectedly, the UACR of these CKD subjects were significantly higher than in non-CKD subjects

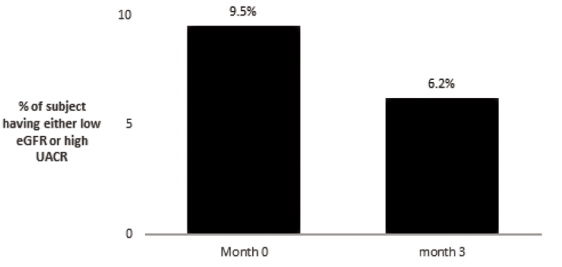

Figure 1. Prevalence of low eGFR <60 or high UACR.
% of subject having either low eGFR <60 cc/minute or high UACR >30 mg/g Cr

(190.1±269 versus 9.87±11.1 mg/g Cr, p<0.001). There were no significant differences in body weight, BMI, serum Cr, eGFR, FBS or LDL among relatives with or without CKD.

Factors associated with CKD

Univariate analysis was conducted to assess association between CKD and risk factors (Table 3). Among the 11 CKD first degree relatives of ESRD patients, three patients (27.3%) were diabetic, four patients (36.4%) were receiving ACEI/ARB, and one patient (9.1%) was taking NSAIDs. The proportions of those with diabetes or history of ACEI/ARB use were significantly higher than the non-CKD family members of ESRD patients (p=0.043 and 0.027, respectively). The proportion of those with history of NSAIDs use (9.1%) was significantly less than that of the non-CKD family members (46.4%), p=0.024.

Discussion

It has been well accepted that genetic factors play a causal role in diabetes and hypertension. Simmons et al and Suzanne et al observe that family members or relatives of diabetic or hypertensive patients have a higher chance to develop diabetes or be hypertensive[22,23]. Moreover, relatives of those who have CKD are also more likely to have higher incidence of CKD[8].

In this communication, stages 1and 2 CKD was found in 6.2% of first-degree family member of ESRD patients. Identification of CKD in the present study was based on albuminuria criteria only. None of those family members with CKD was identified by the low GFR criteria[21]. They were mostly offspring of dialysis patients. The incidence of CKD stages 1 and 2 found in the present study was unexpected slightly lower than that (8.9%) reported in the other randomly clustered study conducted in Thailand[2]. The present study's findings seem to contradict the

Table 2. Demographic characteristics of first degree relatives of ESRD with high UACR (CKD group) and normal UACR (non-CKD group)

Parameters	First degree relatives, Mean ± SD		p-value
	Non-CKD (n = 168)	CKD (n = 11)*	
Bodyweight (kg)	62.9±15	66.7±13.9	0.41
BMI (kg/m^2)	24.0±5.0	26.5±5.1	0.10
Systolic blood pressure (mmHg)	119.2±19.9	138.2±9.9	0.002
Diastolic blood pressure (mmHg)	73.3±13.8	83.0±9.0	0.023
Serum creatinine (mg/dl)	0.73±0.16	0.67±0.12	0.29
eGFR (ml/minute/1.73 m^2 BSA)	103.3±13.0	104.3±16	0.81
FBS (mg/dl)	101.4±26.5	129.0±63.6	0.18
LDL (mg/dl)	130.0±34.2	120.4±34.0	0.36
UACR (mg/g Cr)	9.87±11.1	190.1±269	<0.001
Median (range)		131 (37 to 985)	

SD=standard deviation; CKD=chronic kidney disease; BMI=body mass index; eGFR=estimated glomerular filtration rate; FBS=fasting blood glucose; LDL=low density lipoprotein cholesterol; UACR=urine albumin/creatinine ratio

* Diagnosed by presence of persistent high urine albumin for more than 3 months

All p-value from Student t-test, significant at p<0.05

Table 3. Factors associated with CKD among first degree relatives of ESRD patients (n =179)

	First degree relatives, n (%)		p-value
	Non-CKD (n = 168)	CKD (n = 11)*	
Age (years)			1.00
<50	101 (60.1)	6 (54.5)	
>50	67 (39.9)	5 (45.5)	
Sex			0.73
Male	48 (28.6)	2 (18.2)	
Female	120 (71.4)	9 (81.8)	
Diabetes	11 (6.5)	3 (27.3)	0.043
History of use of ACEI/ARB	17 (10.1)	4 (36.4)	0.027
History of use of NSAIDs	78 (46.4)	1 (9.1)	0.024

CKD=chronic kidney disease; ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blockade; NSAIDs=non-steroidal anti-inflammatory drugs

* Diagnosed by presence of persistent high urine albumin for more than 3 months

previous concept that family history of ESRD is a risk factor of CKD[8]. Perhaps, it could be due to limited number of subjects in the present report. Geographical disparity of the survey area between the two studies could have also been a contributed factor. Moreover, the stratified random cluster method employed in the previous study also differed from non-random recruitment of the relatives of ESRD patients utilized in the present study.

It is interesting that the 11 family members who had CKD found in the present study were identified by presence of high urine albumin. They had higher systolic and diastolic blood pressure, and higher proportion of diabetes than family members without CKD (or albuminuria). All CKD subjects were diagnosed based on high UACR, and not by the low eGFR criteria. The explanation of this finding is not clear. The authors have not studied pathophysiologic mechanism of high blood pressure in our CKD family members. Due to high incidence of diabetes and hypertension as the cause of ESRD, the authors hypothesized that family member of the ESRD patients who also had diabetes (7.8%) or hypertension (11.7%) or both (diabetes mellitus, hypertension include all diet control, and on medication), might have already had subclinical, undetected albuminuria prior to enrollment to the present study. Being lack of renal pathological study, co-existing chronic

glomerulopathy or chronic tubule-interstitial disease as a causal factor could not be ruled out.

In the presence of higher level of systolic and diastolic blood pressure among family members with CKD, they had more frequent history of using ACEI/ARB. Drugs under these two groups were recommended as the first line treatment for essential hypertension[24] diabetic kidney disease[25], or even chronic glomerulopathy[26].

Similarly, family member who were known to be hypertensive or diabetic should have been more cautious about using NSAIDs. Both ESRD patients and their family members at the institution were well informed about deleterious effect of NSAIDs upon kidney function. In addition, the physicians would have been reluctant to prescribe NSAIDs to these CKD patients. Finally, prevalence of CKD among relatives of hemodialysis patients may be underestimated because some family may be CKD but could not participate in the present project due to works or living locations.

Limitation

The present study had some limitations such as relatively small sample size, lack of parallel control group, and evaluation for special groups had selection bias.

Conclusion

Prevalence of CKD among relatives of hemodialysis patients, diagnosed by presence of albuminuria, was 6.2%. The relationship was mostly offspring of dialysis patients. They had higher blood pressure and UACR than those of non-CKD group. History of using ACEI/ARB was more commonly observed and history of using NSAIDs was less observed in the CKD group. Significant high UACR in some portion of the first-degree relatives of ESRD patients should create awareness for early screening of this group and education on CKD should be encouraged for them.

What is already known on this topic?

The prevalence of CKD in Thailand in known. The screening program is usually reserved for those who are at risk of developing CKD. History of CKD among family members is one of the risk factors for developing CKD. In this paper, we studied the prevalence of CKD among family members of ESRD patients in Thailand.

What this study adds?

CKD in this study were identified by presence of high urine albumin. The family members that participated in this study were mostly offspring of dialysis patients. The incidence was similar to the general population. All CKD relatives identified had higher systolic and diastolic blood pressure, and higher proportion of diabetes. We hypothesized that they might already have subclinical, undetected albuminuria prior to enrollment to this study.

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Conflicts of interest

The authors declare no conflict of interest.

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