PREVALENCE AND ASSOCIATED FACTORS IN THE DECLINE OF RENAL FUNCTION AMONG OUTPATIENTS ATTENDING A COMMUNITY HOSPITAL, CENTRAL THAILAND

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Abstract

Introduction: Chronic kidney disease (CKD) is recognized as global public health issue especially affecting developing countries including Thailand. The epidemiologic data in the decline of renal function and the risk factors among Thai patients especially in community hospital settings were limited.

Methods: A cross-sectional study was conducted to identify the prevalence and associated risk factors in the decline of renal function among outpatients in Thaluang Community Hospital, Lop Buri Province, central Thailand, between November 1, 2018 and October 31, 2019. The decline in renal function was defined by glomerular filtration rate (GFR) <60 mL/min/1.73m^2. Multivariate logistic regression analysis was performed to obtain the adjusted odds ratios (AOR) and 95% confidence interval (CI) of the factors related to the decline of renal function.

Results: A total of 874 outpatients participated in the study. The overall prevalence in the decline of renal function (eGFR <60 mL/min/1.73m^2) was 20.3% (95% CI; 17.5%-22.9%). Among male participants, the prevalence in the decline of renal function was 21.1% (95%CI; 16.7%-25.5%) while it totaled 19.7% (95%CI; 16.3%-23.1%) among females. The independent associated factors in the decline of renal function included greater age (AOR 1.07; 95% CI=1.05-1.09), history of NSAIDs used (AOR 2.97; 95% CI=1.85-4.79) and elevated pulse pressure (PP) >75th percentile (AOR 1.64; 95% CI=1.07-2.53)

Conclusion: We reported the prevalence in the decline of renal function among outpatients in a Thai community hospital which was comparable with the national level. Advanced age, history of NSAIDs used and PP were related to reduced kidney function. Therefore, effective health interventions should be conducted especially, appropriate NSAIDs used among outpatients.

Keywords: Decline of renal function, Community hospital, NSAIDs, Pulse pressure, Prevalence, Thailand

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Introduction

At present, chronic kidney disease (CKD) is recognized as a global public health issue and a major health problem, especially affecting developing countries.[1] In Thailand, many people, particularly in rural areas, experience CKD and its complications; moreover, patients with end stage renal disease face difficulties when it comes to hospital costs.[2] In 2009 one related study in Thailand reported the prevalence of CKD stage III-IV was 7.8 and 9.3% among Thai men and women, respectively; additionally, the study demonstrated that the prevalence of CKD was higher in the Bangkok Metropolitan.[3] A 10-year population-based study in Norway demonstrated that mean estimated change in glomerular filtration rate (GFR) was -1.03 ml/min/1.73 m^2/year; additionally, females was associated with slower decline in GFR.[4] Furthermore, patients with rapid decline measured by eGFR tended to increase risk of cardiovascular diseases and mortality.[5]

The risk factors for the decline of renal function include advanced age, noncommunicable diseases such as type 2 diabetes (T2D), hypertension (HT), hyperuricemia, history of kidney stones and history of using traditional medicine.[3,6,7] Moreover, some factors bring about the rapid decrease of eGFR among patients indicating disease progression. [8]

However, epidemiologic data in the decline of renal function (GFR <60 mL/min/1.73m^2) and the risk factors among Thai patients especially in community hospital settings were limited. Therefore, this study collected data from Thaluang Hospital, Lop Buri Province, central Thailand to determine the prevalence in the decline of renal function and associated factors among outpatients attending this community hospital. The results of the present study emphasized that the decline of renal function should be recognized as a serious health problem in Thailand.

Methods

Study designs and subjects

A hospital-based cross-sectional study was conducted to identify the prevalence and associated risk factors for the decline of renal function among outpatients in Thaluang Community Hospital, located in a rural area of Lop Buri Province, about 190 km from Bangkok. Inclusion criteria for the study consisted of patients aged at least 18 years attending the outpatient department of Thaluang Hospital between November 1, 2018 and October 31, 2019. Any patient not presenting a history of serum creatinine testing and eGFR during the period of study was excluded. The study was reviewed and approved by the Royal Thai Army Medical Department Institutional Review Board (approval number S035h/63_Exp).

Data collection

A standardized case report form was used to collect the data from electronic medical records by the investigators. Collected data included (1) demographic data which comprised age, sex, weight, and height (2) risk behaviors and comorbidities including smoking, alcohol consumption, T2D, HT, and dyslipidemia (DLP) (3) systolic blood pressure (SBP), diastolic blood pressure (DBP) and (4) serum creatinine level and estimated GFR. In addition, history of nonsteroidal anti-inflammatory drugs (NSAIDs) used among individuals was reviewed and collected. Body mass index (BMI) was calculated as body weight in kilograms divided by height in meters squared. The pulse pressure (PP) was calculated as the difference between SBP and DBP levels. According to the International Classification of Diseases, Tenth Revision Codes (ICD-10), T2D, HT and DLP were determined by E11, I10-I13 and E78, respectively.[9] Isotope Dilution-Mass Spectrometry traceable enzymatic method was used for the measurement of serum creatinine and eGFR was calculate by CKD-EPI equations.[10] The decline of renal function was defined by eGFR <60 mL/min/1.73m^2.[11]

Statistical analysis

Data were analyzed using StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX, USA: StataCorp LLC. Demographic characteristics were presented using descriptive statistics. Categorical data were presented as number and percentage while continuous data were illustrated as mean and standard deviation (SD). Associated factors of the decline of renal

function were analyzed using binary logistic regression analysis. The magnitude of association was manifested by crude odds ratio (OR) with 95% confidence interval (CI). Multivariate logistic regression analysis was performed to obtain the adjusted odds ratios (AOR) and 95% CI of the factors related to the decline of renal function. A *p*-value less than 0.05 was considered as statistical significance.

Results

A total of 874 outpatients were enrolled in the study. The average age of participants was 60.1±12.9 years. The majority of participants were female (61.6%). The average BMI was 25.3±5.0 kg/m^2. One third of participants (34.4%) had BMI from 25.0 to 29.9 kg/m^2. Among participants, the prevalence of HT and DM were 45.9 and 40.7%, respectively. Almost 14% of the subjects had a history of smoking and alcohol consumption. The demographic data are shown in **Table 1**.

In all 874, 177 outpatients had eGFR <60 mL/min/1.73m^2. The overall prevalence in the decline of renal function was 20.3% (95%CI; 17.5-22.9%). Among male study participants, the prevalence in the decline of renal function was 21.1% (95%CI; 16.7-25.5%) while it totaled 19.7% (95%CI; 16.3-23.1%) among females. The prevalence in decline of renal function, stratified by age groups and sex, is illustrated in **Figure 1.**

Univariate and multivariate logistic regression analysis identifying the associated factors in the decline of renal function are shown in **Tables 2 and 3**. The independent associated factors in the decline of renal function included greater age (AOR 1.07; 95%CI 1.05-1.09), history of NSAIDs used (AOR 2.97; 95%CI 1.85-4.79) and elevated PP >75th percentile (AOR 1.64; 95% CI 1.07-2.53).

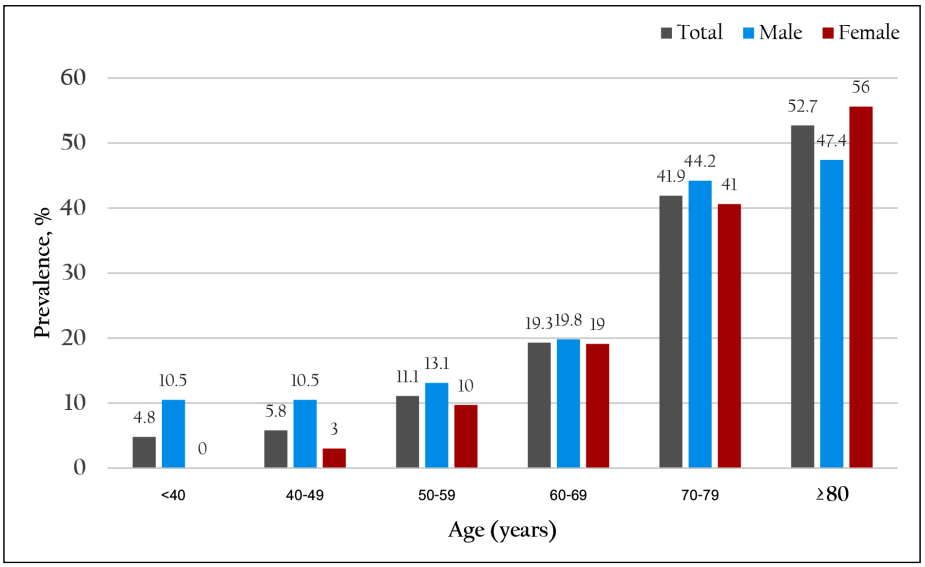

Figure 1. Prevalence of decline of renal function (eGFR<60 mL/min/1.73m^2) stratified by age groups and sex

Table 1. Demographic characteristics of study participants

Characteristics	n (%)
Sex	
Male	336 (38.4)
Female	538 (61.6)
Age (years)	
mean±SD	60.1±12.9

Table 1. Demographic characteristics of study participants (ext.)

Characteristics	n (%)
median (max-min)	60.0 (98-18)
<40	42 (4.8)
40-49	104 (11.9)
50-59	287 (32.8)
60-69	238 (27.2)
70-79	148 (16.9)
≥80	55 (6.3)
Body mass index (kg/m^2)	
mean±SD	25.3±5.0
median (max-min)	25.0 (51.6-12.6)
18.4-22.9	231 (28.3)
<18.5	46 (5.6)
23.0-24.9	137 (16.8)
25.0-29.9	281 (34.4)
≥30.0	121 (14.8)
Smoking	
No	755 (86.4)
Yes	119 (13.6)
Alcohol drinking	
No	753 (86.2)
Yes	121 (13.8)
Hypertension	
No	473 (54.1)
Yes	401 (45.9)
Diabetes mellitus	
No	518 (59.3)
Yes	356 (40.7)
Dyslipidemia	
No	854 (97.7)
Yes	20 (2.3)
History of NSAIDs used	
No	528 (60.3)
Yes	347 (39.7)
Glomerular filtration rate (mL/min/1.73m^2)	
mean±SD	80.3±24.0
median (max-min)	84.5 (147.3-14.6)
>90	358 (41.0)
60-89	339 (38.8)
45-59	99 (11.3)
30-44	46 (5.3)
15-29	30 (3.4)
<15	2 (0.2)

Table 2. Univariate analysis for factors associated with decline of renal function

Factors	GFR <60 mL/ min/1.73 m^2 n (%)	GFR ≥ 60 mL/ min/1.73 m^2 n (%)	Odds Ratio	95% CI	*p*-value
Sex					
Female	106 (19.7)	432 (80.3)	1.00		
Male	71 (21.1)	265 (78.9)	1.09	0.78-1.53	0.609
Age (years)					
mean±SD	68.2±12.1	58.1±12.3	2.85	2.30-3.54	<0.001
<40	2 (4.8)	40 (95.2)	1.00		
40-49	6 (5.8)	98 (94.2)	1.22	0.24-6.32	0.809
50-59	32 (11.2)	255 (88.8)	2.51	0.58-10.88	0.219
60-69	46 (19.3)	192 (80.7)	4.79	1.12-20.55	0.035
70-79	62 (41.9)	86 (58.1)	14.40	3.36-61.91	<0.001
≥80	29 (52.7)	26 (47.3)	22.31	4.90-101.55	<0.001
Body mass index (kg/m^2)					
mean±SD	25.3±4.7	25.3±5.0	1.00	0.96-1.03	0.872
18.4-22.9	52 (22.5)	179 (77.5)	1.00		
<18.5	4 (8.7)	42 (91.3)	0.33	0.11-0.96	0.041
23.0-24.9	33 (24.1)	104 (75.9)	1.09	0.66-1.80	0.729
25.0-29.9	46 (16.4)	235 (83.6)	0.67	0.43-1.05	0.080
≥30.0	21 (17.4)	100 (82.6)	0.72	0.41-1.27	0.258
Smoking					
No	148 (19.6)	607 (80.4)	1.00		
Yes	29 (24.4)	90 (75.6)	1.32	0.84-2.08	0.230
Alcohol drinking					
No	148 (19.7)	605 (80.3)	1.00		
Yes	29 (24.0)	92 (76.0)	1.29	0.82-2.03	0.274
Hypertension					
No	116 (24.5)	357 (75.5)	1.00		
Yes	61 (15.2)	340 (84.8)	0.55	0.39-0.78	0.001
Diabetes mellitus					
No	73 (14.1)	445 (85.9)	1.00		
Yes	104 (29.2)	252 (70.8)	2.52	1.80-3.52	<0.001
Dyslipidemia					
No	177 (20.7)	677 (79.3)	1.00		
Yes	0 (0)	20 (100.0)	N/A	N/A	N/A
History of NSAIDs used					
No	61 (11.6)	466 (88.4)	1.00		
Yes	116 (33.4)	231 (66.6)	3.84	2.71-5.43	<0.001
Pulse pressure (mmHg)					
≤75 percentile (≤63)	113 (16.8)	560 (83.2)	1.00		
>75 percentile (>63)	62 (32.1)	131 (67.9)	2.35	1.63-3.37	<0.001

NSAIDs; non-steroidal anti-inflammatory drugs, CI; confidence interval, SD; standard deviation

Table 3. Multivariate analysis for factors associated with decline of renal function

Factors	Adjusted Odds Ratio	95% CI	*p*-value
Sex			
Female	1.00		
Male	1.06	0.66-1.70	0.815
Age (years)	1.07	1.05-1.09	<0.001
Body mass index (kg/m^2)	1.02	0.98-1.06	0.309
Smoking			
No	1.00		
Yes	1.01	0.42-2.44	0.991
Alcohol drinking			
No	1.00		
Yes	2.02	0.83-4.90	0.119
Hypertension			
No	1.00		
Yes	0.96	0.53-1.72	0.879
Diabetes mellitus			
No	1.00		
Yes	1.28	0.66-2.46	0.464
History of NSAIDs used			
No	1.00		
Yes	2.97	1.85-4.79	<0.001
Pulse pressure (mmHg)			
≤75 percentile (≤63)	1.00		
>75 percentile (>63)	1.64	1.07-2.53	0.024

NSAIDs; non-steroidal anti-inflammatory drugs, CI; confidence interval

Discussion

The present study presented that the prevalence in the decline of renal function (eGFR <60 mL/min/1.73 m^2) among outpatients was 20.3% which was higher than that of the 2010 national survey conducted in Thailand (9.3%).[3] In addition, compared with the prevalence of eGFR <60 mL/min/1.73 m^2 in a Canadian community (14.5%), the prevalence of those in this study was relatively high.[9] According to the hospital-based study, the participants of the present study consisted of a high proportion of patients with T2D and HT, approximately 45%; therefore, their comorbidities may have affected the decline of renal function leading to a high prevalence among the study participants. However, the prevalence in the decline of renal function among study participants was comparable with a related study in the UK reporting a prevalence of 18.2%. [12]

Notably, the prevalence in the decline of renal function stratified by age groups significantly differed. We found that outpatients at higher age tended to be at risk in the decline of renal function. Currently, several countries have become aging societies; thus, the relationships between age and CKD have been reported from many studies. One related study conducted in a semi-urban community in Nigeria found that age was a significant factor of developing CKD.[13] Additionally, recent studies in Thailand and Sri Lanka emphasized that the prevalence of CKD related to aging.[3,14] Similarly, GFR measurement using single-nephron GFR, calculated in a healthy adult population in the US, demonstrated that CKD related to advanced age due to decreased glomerular infiltration in the normal aging process. A steep decline is observed after age 50 years. According to physiological processes, age

is claimed to have immense results in decreased GFR.[13] Many reasons explain this phenomenon. Firstly, long term contact with free radicals and oxidative stress results in declining numbers of normal functional podocyte but increasing numbers of sclerosed glomeruli. Secondly, aging kidneys exhibit structural changes in both micro- and macroanatomical aspects. Microanatomical aspects are explained by increasing sclerosis score among aging adults as a result of atrophy of functioning tubular and interstitial fibrosis and arteriosclerosis while macroanatomical changes are due to decreasing kidney volume, thinner kidney parenchymal and abundance of kidney cysts.[15]

We found that almost 40% of participants presented a history of NSAIDs use; additionally, outpatients with a history of NSAIDs use tended to be at risk of significantly declining renal function. Likewise, one related study in China reported that NSAIDs use related to higher risk of CKD; moreover, using NSAIDs more than 48 months led to reduced renal function. [16] Similarly, a community-based cohort study in Canada reported that exposure to high dose NSAIDs increased the risk of rapidly progressing of CKD.[17]

The phenomenon may be explained by the principal mechanism of NSAIDs action via the cyclooxygenase (COX) inhibitor pathway. COX enzyme inhibition disrupts the conversion of arachidonic acid to different prostaglandins such as prostaglandin E2, prostacyclins and thromboxanes, inducing kidney vasodilatation inhibition and reducing renal perfusion. [18]

Additionally, NSAIDs are one of a risk factors contributing to CKD, especially in advance age. Prolong used of NSAIDs leads to chronic interstitial nephritis, known as CIN, papillary necrosis and finally, CKD.[19,20]

Our study suggested promoting effective interventions such as careful consideration before appropriately prescribing NSADs. In addition, health literacy regarding the risk factors in decline of renal function especially NSAIDs use should be provided to patients.[21]

Our study reported that elevated PP was associated with the decline of renal function. Similarly, the National Institute of Diabetes and Digestive Kidney Diseases registry in the US demonstrated that PP significantly correlated to the decline of GFR levels. [22] Additionally, one related cohort study found that among patients with CKD in stages IV and V, PP more than 80 mmHg constituted a significant predictor for disease progression.[23] PP was identified as a strong independent predictor of rising ambulatory arterial stiffness index. The relationship between elevated PP and decline of renal function may be explained by the process of cardiovascular aging as in arterial stiffness at both macrovascular and microvascular.[24–26] Therefore, PP might constitute a noninvasive proxy indicator for the decline of renal function.[27]

The study employed a cross-sectional survey, making it difficult to establish a cause-and-effect relationship between associated factors and decline of renal function. According to secondary data used for analysis, some variables were incomplete. Another limitation was the small sample size in the study; therefore, the association between well-known risk factors such as T2D, HT, smoking status and outcome could not be presented. The results of our study may not be generalized to the whole country but may reflect the real situation of outpatients attending a Thai community hospital.

To our knowledge, this study is the latest study of the decline of renal function among patients attending a Thai community hospital. The results emphasized that Thailand, a developing country, is experiencing a serious public health burden. The decline of renal function including CKDs should be recognized as a serious health problem. The Ministry of Public Health should raise more awareness of this issue among the national population to prevent the disease and alleviate its complications.

Conclusion

The prevalence of the decline of renal function among outpatients in a Thai community hospital was higher than that at the national level. It indicated that this constituted an essential health problem not only in urban areas but also in rural communities. Advanced age, a history of NSAIDs use and PP were related to reduced

kidney function. Additionally, effective health interventions should be conducted especially, to ensure appropriate NSAIDs use among patients.

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