GLOMERULAR FILTRATION RATE IN ELDERLY PATIENTS WITH HYPERTENSION AND DIABETES IN MEKONG DELTA, VIETNAM

Tran Thai Thanh Tam*, Dinh Thi Hue, Nguyen Thang, Nguyen Phan Hai Sam, Pham Kieu Anh Tho, Nguyen Trung Kien

Can Tho University of Medicine and Pharmacy

**Corresponding author*: *ttttam@ctump.edu.vn*

ABSTRACT

Background: *Old age has been a risk factor for chronic kidney diseases (CKD). Some comorbidities such as hypertension and diabetes can exacerbate a decrease of glomerular filtration rate (GFR). Therefore, the overall number of functioning nephrons will decrease rapidly.* ***Objectives:*** *To assess the mean GFR, prevalence, stage of CKD, and the related risk factors in the geriatric population with hypertension and diabetes in Mekong Delta, Vietnam.* ***Materials and methods:*** *This is a prospective cross-sectional study of 98 elderly patients aged ≥ 60 years with hypertension and diabetes at Can Tho University Hospital from September 2017 to May 2018. eGFR was GFR estimated by CKD-EPI creatinine equation 2009, and CKD was classified by KDIGO 2009.* ***Results:*** *The mean eGFR was 62.2±25.7mL/min/1.73m^2. The prevalence of eGFR < 60mL/min/1.73m^2 was 48% in which CKD stage 3a, stage 3b, stage 4, and stage 5 were 20.4%, 13.3%, 10.2%, and 4.3%, respectively. The elderly patients with hypertension and diabetes had higher odds of eGFR < 60ml/min/1.73m^2 when they were female (OR=2.85; 95%CI= 1-8.11), or had age >70 years (OR=2.28; 95%CI = 1.02-5.13), blood pressure > 140/90 mmHg (OR=2.87; 95%CI = 1.25-6.61), HbA1C ≥ 7.5% (OR=3.11; 95%CI=1.35-7.16), glycemia > 7.2mmol/L (OR=2.65; 95%CI=1.15-6.10), abdominal obesity (OR=4.07; 95%CI =1.23-13.44), time after diabetes recognition > 5 years (OR=3.84; 95% CI =1.28-11.53), tobacco intake (OR=10; 95%CI=1-110.28), p <0.05 for all.* ***Conclusions:*** *A high prevalence of eGFR below 60 mL/min/1.73m^2 among the geriatric population in Mekong Delta, Vietnam, with hypertension and diabetes was found. It is crucial to have early detection of CKD and its relative risks to prevent the progression in patients with CKD.*

Keywords: *eGFR, elderly patients, diabetes, hypertension, Vietnamese*.

I. INTRODUCTION

Chronic kidney disease (CKD) is a global public health issue. Data from the National Health and Nutrition Examination Survey (NHANES) showed a CKD prevalence in the period 2011-2014 of 6.6%, 10.6% and 32.6% in age groups of 20–39, 40–59 and ≥ 60 years, respectively [8]. The decline of glomerular filtration rate (GFR) with aging usually begins after 30-40 years of age, and it may hasten after the age of 50-60 years. This decline is considered as a consequence of organ senescence and related to changes in renal structure [3], [17]. Old age was found to be a risk factor for CKD. However, some comorbidities such as hypertension and diabetes can exacerbate GFR decline [1]. Therefore, the overall number of functioning nephrons will decrease rapidly.

Since the first study of Nathan Shock, et al. on GFR in elderly people in 1945, plenty of reports have been made on these aging subjects by measuring the clearance of inulin or creatinine, or even estimated GFR [13], [4]. However, the epidemiology of CKD in Vietnamese older patients with hypertension and diabetes is not well documented. The aim of this study was to assess the mean GFR, prevalence, and stage of chronic kidney disease (CKD) and its related risk factors in the geriatric population with hypertension and diabetes in Mekong Delta, Vietnam.

II. MATERIALS AND METHODS

2.1. Study population and setting

In this study, 156 patients older than 60 years old with hypertension and diabetes in

Mekong Delta, Vietnam, visited the Health Examination Center, Hospital of Can Tho University of Medicine and Pharmacy between September 2017 and May 2018, and initially enrolled in this cross-sectional study. Among them, 98 patients who were prospectively followed up at the center for at least three months were selected. We excluded 58 patients with a monitored period of less than 3 months, no available data of body weight and height, serum creatinine, blood pressure, glucose concentration, history of primary kidney diseases, hypertension, or diabetes.

All patients with inclusion and without exclusion criteria were eligible in this research. Hypertension was defined according to the Joint National Committee 7 report (JNC 7) [10], or patients with a previous diagnosis of hypertension. Diabetes was diagnosed according to the American Diabetes Association 2020 (ADA 2020) by fasting plasma glucose (FPG) of $\geq$ 7 mmol/L, HbA1C $\geq$ 6.5%, or symptoms of hyperglycemia plus a random plasma glucose $\geq$ 11.1 mmol/L [5], or patients who had a previous diagnosis of diabetes. CKD was classified based on the estimated glomerular filtration rate (eGFR). Staging of CKD was defined as G3a, G3b, G4, and G5 when eGFR was 45-59, 30-44, 15-29, and <15 ml/min/1.73m^2, respectively [8]. Overweight and obesity were defined by body mass index (BMI) of $\geq$ 23 kg/m^2 and 25 kg/m^2, respectively. Abdominal obesity was classified by waist-hip ratio (WHR) > 0.9 for men and > 0.8 for women [15]. Tobacco intake was defined as being smoking.

2.2. Study design and contents

The physical examination and interview were carried out during outpatient visits to determine the history of hypertension, diabetes, dyslipidemia, and tobacco intake. After fasting overnight, blood sampling concluding glycemia, HbA1c, blood urea nitrogen (BUN), serum creatinine (Scr) was performed. Scr level was determined using standard laboratory methods.

Blood pressure (BP) was measured by using a properly sized blood pressure cuff and a mercury column sphygmomanometer in the sitting posture after a 10 to 15-minute rest. Height and body weight, waist and hip circumference were measured. BMI was calculated as body weight in kilograms divided by the square of height in meters. WHR was measured as waist circumference divided by hip circumference. GFR was estimated by using chronic kidney disease (CKD-EPI) equation based on serum creatinine [8]:

For women with a Scr $\leq$ 0.7, $144\times(Scr/0.7)^{-0.329}\times0.993^{age}$;

For women with a Scr > 0.7, $144\times(Scr/0.7)^{-1.209}\times0.993^{age}$;

For men with a Scr $\leq$ 0.9, $141\times(Scr/0.9)^{-0.411}\times0.993^{age}$;

For men with a Scr > 0.9, $141\times(Scr/0.9)^{-1.209}\times0.993^{age}$.

2.3. Statistical Analysis

Data were analyzed using version 16.0 of SPSS statistical program. The normality of the distributions of variables was checked by the Kolmogorov Smirnov test. Continuous variables were expressed as mean ± SD or median (IQR) for skewed variables and categorical variables as percentages for descriptive statistics. The Kruskal-Wallis test is used to assess for significant differences on a continuous dependent variable with distribution free by a categorical independent variable (with two or more groups). A one-way ANOVA was used to compare the means from more than two independent groups using the F- distribution. The significance of the difference between the two groups was determined by chi-square test for categorical variables and *t*-test for continuous variables.

Odds ratio (OR) and 95% confidence interval (CI) were calculated. P-values < 0.05 were considered statistically significant.

2.4. Ethics Approval

The protocol of this study was approved by the medical ethics committee of the Hospital of Can Tho University of Medicine and Pharmacy. Each patient had signed an informed consent form before participating in the research.

III. RESULTS

Table 1. Study population characteristics

Variable	Mean ± SD	Max	Min
Weight (Kg)	55.54±9.68	80	36
Height (cm)	157.28±6.83	178	145
BMI (Kg/m^2)	22.47±3.72	34.2	15.2
Waist circumference (cm)	85.73±11.69	130	60
Hip circumference (cm)	88.59±8.46	117	70
WHR	0.97±0.08	1.3	0.79

BMI, body mass index; SD, standard deviation; WHR, waist-hip ratio.

Table 2. Renal function according to age groups in elderly patients with hypertension and diabetes

Variable		Median (IQR) or mean ± SD	Max	Min	p
Serum urea (mmol/L) Median (IQR)	60-69	6.3 (5.1-9.0)	22.6	1.4	0.066[a]
	70-79	5.6 (4.0-8.5)	17.2	2.6	
	≥ 80	9.3 (5.1-11.0)	18.8	3.5	
	Total	6.4 (4.7-9.5)	22.6	1.4	
Serum creatinine (µmol/L) Median (IQR)	60-69	87.1 (62.2-108.4)	375	49	0.342[a]
	70-79	83.8 (61.0-119.7)	197.9	51	
	≥ 80	103.6 (73.0-139.1)	188	43	
	Total	85.2 (62.9-117.7)	375	43	
eGFR (mL/min/1.73m^2) Mean± SD	60-69	66.7±27.1	98.8	10.6	0.11[b]
	70-79	61.2±23.3	99.1	23.5	
	≥ 80	52.2±24.0	91.9	21.3	
	Total	62.2±25.7	99.8	10.6	

eGFR, estimated glomerular filtration rate; IQR, interquartile range; SD: standard deviation; [a]Kruskal-Wallis Test; [b]One Way Anova.

Table 3. Related risk factors of CKD in elderly patients with hypertension and diabetes

Risk factors	OR	[95% CI]	p
Sex (Female)	2.85	1-8.11	0.045
Age > 70 years	2.28	1.02-5.13	0.044
Uncontrolled hypertension	2.87	1.25-6.61	0.01
HbA1C ≥ 7.5%	3.11	1.35-7.16	0.007
FPG >7.2 mmol/L	2.65	1.15-6.10	0.02
History of BP >5 years	1.34	0.39-4.54	0.641
History of diabetes (>5 years)	3.84	1.28-11.53	0.01
BMI (≥ 23 kg/m^2)	0.57	0.25-1.30	0.18
Abdominal obesity	4.07	1.23-13.44	0.019
Tobacco intake	10	1-110.28	0.043

BMI, body mass index; BP, blood pressure; FPG, fasting plasma glucose.

Among 98 patients included, 21 (21,4%) were males, 77 (78,6%) females. The mean age ±SD was 72.2±8.6 years (60-89 years). The mean GFR was 62.2±25.7 mL/min/1.73m^2, (10.6-99.8mL/min/1.73m^2). The prevalence of CKD was 48%, in which 20.4%, 13.3%, 10.2% and 4.1% patients were in CKD stages of 3a, 3b, 4 and 5, respectively. We presented the study population characteristics in **Table 1**, renal function in **Table 2**, and related risk factors of CKD in **Table 3**.

IV. DISCUSSION

Nearly half of the patients who had eGFR under 60mL/min/1.73m^2 were diagnosed with CKD from stage 3a to end-stage of renal disease. The risk factors significantly related to GFR were group age > 70 years, uncontrolled hypertension, history of BP > 5 years, and abdominal obesity.

The decline of eGFR in elderly patients appears to be a part of the normal physiologic process of kidney senescence. Therefore, chronic kidney disease is common in the geriatric population. It can be diagnosed in approximately 25% of people aged 65–74 years, and in > 50% of those aged > 75 years [2]. The decrease of GFR can be affected by several factors, namely genetic, ethnic, environment, and co-morbidities such as diabetes mellitus and hypertension [7], [14]. With aging, most of the population tends to have diabetes and hypertension; it is well established that these diseases are the most common causes of end-stage renal disease in the elderly.

According to Improving Global Outcomes (KDIGO) practice guidelines, CKD is defined as a GFR < 60 ml/min/1.73m^2 or the presence of kidney damage (abnormal urinalysis, kidney imaging, or renal biopsy) that persists for ≥ 3 months. However, in this study, we considered CKD as eGFR CKD-EPI < 60 ml/min/1.73 m^2. Besides, how to choose a precise eGFR for this population was also a challenge. Up to now, studies on CKD prevalence in the geriatric population are rather scarce in developing countries, where the older population as well as prevalence of diabetes, hypertension are rising [9]. Few studies designed based on the elderly population have shown that a diversity of CKD prevalence varied from 23.4 to 58.5% [16]. In our study, the prevalence of CKD in elderly patients with hypertension and diabetes mellitus was 48%. A part of this discrepancy may be explained by the use of different equations to estimate GFR, the differences in the age of the elderly population and comorbidities. A study on 800 Italian aged 85 or older was done to evaluate five equations of eGFR, including Cockcroft-Gault, BIS, CKD-EPI, MDRD, and Mayo Clinic equations [11], and its result showed a wide variation in the eGFR prevalence of 90.7%, 84.4%, 53.6%, 48.1%, and 23.3%, respectively [11]. In the Berlin Initiative Study (BIS) including 2069 subjects aged ≥ 70 years, the prevalence of GFR < 60 mL/min/1.73m^2 ranged from 37.1% to 61.7% using various eGFR equations, in which eGFR obtained by MDRD equation gave the lowest prevalence value, while those obtained by BIS1 showed the highest prevalence value [6]. According to Giuseppina T. Russo *et al.*, the percentage of elderly people with diabetes and having eGFR CKD-EPI <60ml/min/1.73m^2 was 21.7% and 44.3% in the group aged 65-75 years and 75-85 years, respectively [12].

The limitation of our study was that we diagnosed and classified CKD based on a single decreased eGFR value without in combination with another proof of kidney damage. In addition, the best eGFR for the geriatric population is not confirmed, and thus it is still an important and difficult question. The eGFR based on CKD-EPI equation in our study

might be more precise as we had combined serum cystatin C and serum creatinine. To the best of our knowledge, no comparable study on GFR in elderly patients in Vietnam has been found. Therefore, the importance of our study was to provide data on eGFR and the prevalence of CKD in the geriatric population with hypertension and diabetes. This allows running a program to minimize the risk factors and prevent the progress to the end stage of renal disease in the population in the developing countries, especially in Vietnam. Moving forward, to control the growing public health issue of CKD, it calls for other studies on kidney estimated functions and how to prevent this disease effectively in Vietnam.

V. CONCLUSIONS

The geriatric population with hypertension and diabetes with eGFR below 60mL/min/1.73m^2 had a high average prevalence of 48%. Low GFR in older patients is recommended as a strong indicator of the presence of concomitant kidney disease. It is crucial to have early detection of CKD and its relative risks in order to prevent the progression in patients with CKD.

REFERENCES

1. Abdulkader RCRM, Burdmann EA, Lebrão ML, Duarte YAO, Zanetta DMT (2017), "Aging and decreased glomerular filtration rate: An elderly population-based study", *PLoS ONE*, 19, 12(12).
2. Couser WG, Remuzzi G, Mendis S, Tonelli M (2011), "The contribution of chronic kidney disease to the global burden of major non-communicable diseases", *Kidney Int*, 80, pp. 1258–1270.
3. Darmady EM, Offer J, Woodhouse MA (1973), "The parameters of the aging kidney", *J Pathol*, 109, pp. 195–207.
4. Davies DF, Shock NW (1950), "Age changes in glomerular filtration rate, effective renal plasma flow and tubular excretory capacity in adult males", *J Clin Invest*, 29, pp. 496 –504.
5. Diagnosis and classification of diabetes mellitus (2012), *Diabetes Care*, 35, S64–S71.
6. Ebert N, Jakob O, Gaedeke J, van der Giet M, Kuhlmann MK, Martus P *et al.* (2017), "Prevalence of reduced kidney function and albuminuria in older adults: the Berlin Initiative Study", *Nephrol Dial Transplant*, 32, pp. 997–1005.
7. Grams ME, Chow EK, Segev DL, Coresh J (2013), "Lifetime incidence of CKD stages 3–5 in the United States", *Am J Kidney Dis*, 62, pp. 245–252.
8. Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, Kurella Tamura M, Feldman HI (2014), "KDIGO Clinical Practice Guideline for the Evaluation and Management of CKD", *Am J Kidney Dis*, 63, pp. 713–735.
9. Jha V, Garcia-Garcia G, Iseki K *et al.* (2013), "Chronic kidney disease: global dimension and perspectives", *Lancet*, 382, pp. 260–272.
10. Lenfant C, Chobanian AV, Jones DW, Roccella EJ (2003), "Seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7): resetting the hypertension sails", *Hypertension*, 41, pp. 1178–1179.
11. Mandelli S, Riva E, Tettamanti M, Detoma P, Giacomin A, Lucca U (2015), "Mortality prediction in the oldest old with five different equations to estimate glomerular filtration rate: The Health and Anemia Population-based Study", *PLoS One*. 10.
12. Russo GT, De Cosmo S, Viazzi F, Mirijello A, Ceriello A, Guida P, Giorda C, Cucinotta D, Pontremoli R, Fioretto P et al. (2018), "Diabetic kidney disease in the elderly: prevalence and clinical correlates, *BMC Geriatr*, 18, 38.
13. Shock N (1946), "Renal function test in aged males". *Geriatrics*, 1, pp. 232–239.

14. United States Renal Data System (2014), "Annual data report: epidemiology of kidney disease in the United States", *Bethesda: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases*.
15. World Health Organization (WHO) (2008), "Waist Circumference and Waist-Hip Ratio", *Report of WHO Expert Consultation*.
16. Zhang QL, Rothenbacher D (2008), "Prevalence of chronic kidney disease in population-based studies: Systematic review", *BMC Public Health*, 8, 117.
17. Zhou XJ, Rakheja D, Yu X, Saxena R, Vaziri ND, Silva F (2008), "The aging kidney". *Kidney Int.* 74, pp. 710–720.

(Received: 10/3/2021 – Accepted: 28/6/2021)