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RESEARCH ARTICLE

Prevalence of diabetic nephropathy among Chinese patients with type 2 diabetes mellitus and different categories of their estimated glomerular filtration rate based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation in primary care in Hong Kong: a cross-sectional study

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Abstract

Purpose To evaluate the prevalence of diabetic nephropathy and different categories of estimated glomerular filtration rate (eGFR) as calculated by the CKD-EPI equation among Chinese patients with type 2 diabetes in primary care in Hong Kong. The associated factors of diabetic nephropathy were also analyzed.

Methods A cross-sectional study was conducted in 35,109 Chinese patients with type 2 diabetes followed up in all General Outpatient Clinics in a Hospital Authority cluster and had undergone comprehensive diabetic complication assessment from April 2013 to March 2016. The GFR was estimated by the CKD-EPI equation. Logistic regression was used to analyze the associated factors of diabetic nephropathy.

Results The prevalence of diabetic nephropathy (with either or both albuminuria and impaired eGFR), impaired eGFR (with or without albuminuria) and albuminuria (with or without impaired eGFR) was 31.6%, 16.9% and 22.0% respectively. The prevalence of eGFR categories 1, 2, 3, 4 and 5 was 36.0%, 47.1%, 15.7%, 1.1% and 0.1% respectively. The comorbidity with hypertension or presence of other diabetic microvascular or macrovascular complications including diabetic retinopathy, peripheral neuropathy, peripheral vascular disease, history of stroke and history of ischemic heart disease had strong association with diabetic nephropathy. Obesity, smoking, suboptimal control of blood pressure, hemoglobin A1c and non-high density lipoprotein cholesterol were also significantly associated with diabetic nephropathy.

Conclusions Diabetic nephropathy was common among Chinese patients with type 2 diabetes in primary care in Hong Kong. Early identification and control of the modifiable risk factors are of upmost importance in preventing the complication.

Keywords Type 2 diabetes · Diabetic nephropathy · Glomerular filtration rate · Primary care

Introduction

Diabetes mellitus is a major public health problem. The World Health Organization reported that the global prevalence of diabetes was around 9% among adults aged above 18 years in 2014 [1]. According to the International Diabetes Federation, the number of people with diabetes is expected to increase above 500 million by 2030 [2]. Diabetes occurs in about 10% of Hong Kong population and is one of the most common chronic diseases encountered in primary care. About 2% of people aged less than 35 years and more than 20% of those older than 65 years are affected by the disease [3].

Diabetes is the leading cause of chronic kidney disease (CKD) worldwide [4]. Diabetic nephropathy is defined as diabetes with the presence of albuminuria, impaired glomerular filtration rate (GFR), or both [5]. The analyses of a national survey in 2011 estimated that among the US adults diagnosed with diabetes, the prevalence of diabetic nephropathy,

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impaired GFR (with or without albuminuria) and albuminuria (with or without impaired GFR) was 34.5%, 17.7% and 23.7% respectively [6]. A study in China reported similar prevalence of diabetic nephropathy (31.0%) and albuminuria (28.9%) [7]. According to the Hong Kong Renal Registry Report 2012, diabetes was the most common cause (45%) of end-stage renal failure (ESRF) [8]. Given the projected increase in the number of people diagnosed with diabetes, the number of people with ESRF due to diabetic nephropathy may increase significantly over the next few decades and impose heavy burden on our healthcare system.

Meta-analyses have shown that impaired GFR and presence of albuminuria are independent risk factors for progressive CKD, ESRF, all-cause mortality and cardiovascular mortality in general population [9, 10]. It has been demonstrated that therapeutic interventions can be implemented to ameliorate the onset and course of diabetic nephropathy significantly if the condition is recognized at its initial stages [11–13]. Thus, early and accurate detection of impaired GFR and albuminuria in diabetic patients is of upmost importance for initiating and optimizing treatment to slow down the progression of kidney failure, assessing and modifying other comorbid conditions, and reviewing prescription of renally excreted or nephrotoxic drugs [14]. Although the Modification of Diet in Renal Disease (MDRD) Study equation had been recommended for estimating GFR for long time [5], it is known that it would underestimate the GFR in patients with normal or near normal kidney function as it was initially derived from data acquired from patients with CKD [15, 16]. It is also only valid if the age is from 18 to 85 years old [17]. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) had proposed a new equation in 2009 using the same four variables (age, sex, race, and serum creatinine level) as the MDRD Study equation [18]. The new equation is applicable in a wider age range including those people older than 85 years old [17]. The CKD-EPI equation has been shown to estimate GFR more precisely compared with the MDRD Study equation among various study populations including Chinese and different clinical conditions including patients with hypertension and diabetes [18–21]. There is also lower bias especially at higher estimated GFR when using the CKD-EPI equation and thus leads to fewer false positive diagnosis of CKD [18]. Moreover, studies have demonstrated that the CKD-EPI equation is more accurate in categorizing the clinical risk, including acute myocardial infarction, end-stage renal disease, stroke and all-cause mortality [22, 23]. Therefore, the CKD-EPI equation is more suitable for estimating kidney function than the MDRD Study equation in primary care in which more patients have normal or near normal renal function. The National Institute for Health and Care Excellence (NICE) 2014 guideline for CKD also recommended the use of CKD-EPI to estimate GFR [24]. Nevertheless; the CKD-EPI equation is not yet widely adopted in most Hospital Authority clinical settings in current practice.

Increased systolic blood pressure (BP), non-high density lipoprotein (non-HDL) cholesterol, poor glycemic control, long duration of diabetes, smoking history, older age, higher body mass index (BMI), previous retinopathy and previous sensory neuropathy have all been found to be risk factors of diabetic nephropathy [25–29]. Moderate alcohol consumption was reported to have association with reduced risk of diabetic nephropathy [30]. However, most of the evidence was derived from non-Chinese populations. The association of these risk factors in Chinese patients is yet to be explored.

To our knowledge, there was no published data regarding the prevalence of diabetic nephropathy and different categories of GFR among Chinese diabetic patients using the CKD-EPI equation in primary care in our locality.

This study therefore aimed to evaluate the prevalence of diabetic nephropathy and different categories of estimated GFR (eGFR) in Chinese diabetic patients in primary care in Hong Kong by using the new CKD-EPI equation. The associated risk factors would also be investigated. The results would provide us important information about the epidemiology of diabetic nephropathy in primary care in Hong Kong. This would be useful for devising the long-term management policy for our diabetic patients in primary care in order to reduce the incidence of ESRF caused by diabetic nephropathy.

Materials and methods

Study design

This was a cross-sectional study. The study was carried out in a local cluster of Hospital Authority, which covered two of the eighteen districts and around 15% of total population of Hong Kong. According to Hospital Authority statistics, the local cluster with eight General Out-patient Clinics (GOPCs) served about 42,000 diabetic patients in year 2016. All patients attending the GOPCs in the cluster who had undergone the comprehensive diabetic complication assessment program from 1st April 2013 to 31st March 2016 would be included. The inclusion and exclusion criteria were summarized as below:

Inclusion criteria:

1. Patients with diagnosis of type 2 diabetes who had undergone the diabetic complication assessment program within the study period

Exclusion criteria:

1. Non-Chinese patients
2. Patients with diabetes not confirmed
3. Patients with type 1 diabetes
4. Patients with renal transplant
5. Patients undergoing peritoneal dialysis or hemodialysis

6. Patients with missing serum creatinine measurement
7. Patients with missing urinary albumin creatinine ratio (ACR) measurement

A list of patients fulfilling the inclusion criteria was generated from the Hospital Authority Clinical Data Analysis and Reporting System for analysis. The sampling frame would be able to include all the eligible subjects being followed up in the participating clinics since each subject would attend the comprehensive diabetic complication assessment program at least once every 3 years and all patients newly diagnosed with diabetes mellitus would receive the comprehensive complication assessment within 6 months of diagnosis. The latest complication assessment results would be used for analysis in patients received more than one complication assessment within the study period.

Procedure

Collected variables included age, gender, blood pressure, BMI, current smoking and drinking status, duration of diabetes, co-morbidities including hypertension, ischemic heart disease and stroke, complications including retinopathy, peripheral neuropathy and peripheral vascular disease. Collected laboratory test results included urine ACR, serum creatinine, glycated hemoglobin A1c (HbA1c), total cholesterol and high density lipoprotein (HDL) cholesterol. The GFR was subsequently estimated by the CKD-EPI equation as below.

CKD-EPI equation [18]:

$$\mathrm{eGFR} = 141 \times \min\left(\mathrm{Scr}/\kappa, 1\right)^{\alpha} \times \max\left(\mathrm{Scr}/\kappa, 1\right)^{-1.209} \times 0.993^{\mathrm{Age}} \times 1.018\ [\text{if female}]\ \mathrm{ml/min/1.73m^2}$$

Scr is serum creatinine in mg/dL, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and − 0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

The GFR categories (category 1: GFR ≥ 90 ml/min/1.73 m^2; category 2: GFR 60 to 89 ml/min/1.73 m^2; category 3: GFR 30 to 59 ml/min/1.73 m^2; category 4: GFR 15 to 29 ml/min/1.73 m^2; and category 5: GFR <15 ml/min/1.73 m^2) were classified according to the NICE guideline [24].

Diabetic nephropathy was defined as diabetes with the presence of albuminuria, impaired GFR, or both [5]. Impaired GFR was defined as GFR less than 60 ml/min/1.73 m^2 [5]. Albuminuria was defined as a spot urine ACR >2.5 mg/mmol for male and > 3.5 mg/mmol for female [31].

Non-HDL cholesterol was calculated by subtracting HDL-cholesterol from total cholesterol.

Diabetic retinopathy grading was performed with use of fundi photos by trained optometrists. The presence of diabetic peripheral neuropathy was defined as abnormal vibration threshold (more than 25 V) detected by a biothesiometer on the big toe or abnormal light touch perception tested with a 10-g monofilament at 4 plantar sites [32]. The presence of peripheral vascular disease was defined as abnormal pedal pulses detected by palpation and doppler ultrasound.

Outcomes

Primary outcomes were the prevalence of diabetic nephropathy based on the presence of albuminuria and/or impaired eGFR by using the CKD-EPI equation and the prevalence of different categories of eGFR among Chinese patients with type 2 diabetes in our GOPCs. Secondary outcome was the associated risk factors for development of diabetic nephropathy.

Statistical analysis

SPSS (Version 21.0) was used for statistical analysis. Continuous variables would be presented as means ± standard deviation (SD) and compared with Student's t test. Skewed data would be presented in median and compared with Mann-Whitney test. Categorical variables would be presented as percentages and compared with Chi-square test. Logistic regression would be used to assess factors associated with diabetic nephropathy. A p value <0.05 would be considered statistically significant.

Results

Study population

There were 35,835 patients underwent the comprehensive diabetic complication assessment program within the study period. 726 (2%) patients were excluded as shown in Fig. 1. A total of 35,109 individuals were included in the final analysis.

The demographic and clinical characteristics of all individuals included in the study were shown in Table 1. The mean age of our patients was 65.3 years and there were more female patients (53.4%). Most of the patients were non-smokers (69.7%) and non-drinkers or ex-drinkers (80.0%). The mean duration of diabetes was 9.1 years. 81.2% of patients had hypertension. 5.9% and 6.1% of patients had already developed ischemic heart disease and stroke respectively. The mean systolic and diastolic blood pressure was 130 and 73 mmHg and nearly half of the patients (46.7%) had blood pressure controlled to less than 130/80 mmHg. About three-quarters (74.6%) of patients were overweight or obesity. 61.7% of patients had their HbA1c levels controlled to less than 7% (53 mmol/mol) while 28.9% of patients had non-HDL cholesterol levels less than 2.5 mmol/L. Diabetic retinopathy,

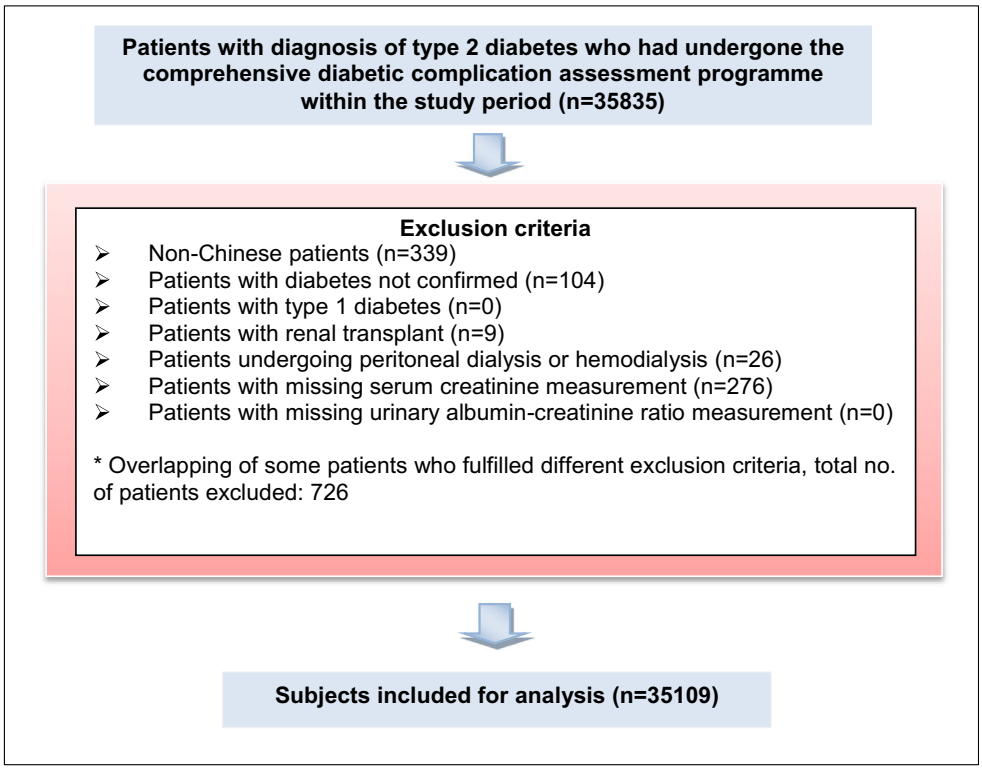

Fig. 1 Flow chart showing the exclusion criteria

peripheral neuropathy and peripheral vascular disease was present in 36.4%, 9.7% and 0.1% of patients respectively.

The prevalence of diabetic nephropathy

The prevalence of diabetic nephropathy, impaired eGFR (with or without albuminuria) and albuminuria (with or without impaired eGFR) was 31.6%, 16.9% and 22.0% respectively. More than four-fifths of patients had normal eGFR as estimated by the CKD-EPI equation (category 1: 36.0% and category 2: 47.1%). The prevalence of eGFR category 3 was 15.7%. A minority of patients had eGFR belonged to category 4 (1.1%) and category 5 (0.1%) (Table 2).

Factors associated with diabetic nephropathy

32,375 patients with no missing clinical parameters or laboratory data were included for analysis of factors associated with diabetic nephropathy in the logistic regression. The results revealed that the presence of other diabetic microvascular or macrovascular complications had strong association with diabetic nephropathy (proliferative diabetic retinopathy [Odd ratio (OR) 6.52, $p < 0.001$], peripheral vascular disease [OR 2.19, $p = 0.023$], stroke [OR 1.5, $p < 0.001$], peripheral neuropathy [OR 1.48, $p < 0.001$] and ischemic heart disease [OR 1.22, $p < 0.001$]). The presence of hypertension was also significantly associated with diabetic nephropathy [OR 1.99, $p < 0.001$]. Other demographic or clinical parameters like older age [OR 1.06, $p < 0.001$], male patients [OR 1.27, $p < 0.001$], smokers [OR 1.49, $p < 0.001$], longer duration of diabetes [OR 1.03, $p < 0.001$] and obesity [OR 1.51, $p < 0.001$] were also found to be associated with diabetic nephropathy. The risk of diabetic nephropathy in patients with suboptimal blood pressure, HbA1c and non-HDL cholesterol control was 1.26, 1.28 and 1.20 times respectively when compared with patients with those parameters controlled to target. ($p < 0.001$) (Table 3).

On the other hand, social drinking [OR 0.89, $p = 0.002$] and current drinking [OR 0.72, $p < 0.001$] were found to have significant negative association with diabetic nephropathy (Table 3).

Discussion

The overall prevalence of diabetic nephropathy in type 2 diabetes patients in our study was 31.6%. Albuminuria was present in 22.0% of patients while 16.9% of patients had impaired eGFR.

Similar prevalence of diabetic nephropathy, albuminuria and impaired eGFR were also found in other studies in China (diabetic nephropathy 31.0%, albuminuria 28.9%) [7] and US (diabetic nephropathy 34.5%, albuminuria 23.7%, impaired eGFR 17.7%) [6]. Two primary care studies in Spain and a Mediterranean area also showed comparable prevalence of diabetic nephropathy to our results (27.9% and

Table 1 Demographic data and clinical characteristics of patients (N = 35109)

	Mean (SD)	Number (%)
Age (years)	65.3 (11.4)	
< 40		428 (1.2)
40–49		2192 (6.3)
50–59		8512 (24.2)
60–69		11,419 (32.5)
70–79		8424 (24.0)
≥ 80		4134 (11.8)
Sex		
Male		16,370 (46.6)
Female		18,739 (53.4)
Smoking status		
Non-smoker		24,472 (69.7)
Ex-smoker		6978 (19.9)
Smoker		3641 (10.3)
Unknown		18 (0.1)
Drinking status		
Non and ex-drinker		28,099 (80.0)
Social-drinker		6043 (17.2)
Drinker		895 (2.6)
Unknown		72 (0.2)
Duration of diabetes (years)	9.1 (6.5)	
< 5		10,022 (28.5)
5–10		12,910 (36.8)
> 10		12,140 (34.6)
Unknown		37 (0.1)
History of hypertension		
Yes		28,506 (81.2)
No		6603 (18.8)
History of ischemic heart disease		
Yes		2091 (5.9)
No		32,785 (93.4)
Unknown		233 (0.7)
Yes		2140 (6.1)
No		32,791 (93.4)
Unknown		178 (0.5)
Systolic blood pressure (mmHg)	130.1 (15.2)	
< 130		18,354 (52.3)
130–139		8013 (22.8)
≥ 140		8287 (23.6)
Unknown		455 (1.3)
Diastolic blood pressure (mmHg)	73.0 (9.8)	
< 80		26,220 (74.7)
80–89		6726 (19.1)
≥ 90		1708 (4.9)
Unknown		455 (1.3)
Control of BP		
Below target (BP < 130/80 mmHg)		16,398 (46.7)
Above target (BP ≥ 130/80 mmHg)		18,256 (52.0)
Unknown		455 (1.3)
Body mass index (kg/m^2)	25.7 (4.0)	
< 23		8769 (25.0)
23–24.9 (overweight)		7526 (21.4)
≥ 25 (obesity)		18,679 (53.2)
Unknown		135 (0.4)
HbA1c (% / mmol/mol)	7.0 (1.1)	
< 6.5 / < 48		11,757 (33.5)
6.5–6.9 / 48–52		9896 (28.2)
≥ 7 / ≥ 53		13,259 (37.8)
Unknown		197 (0.5)
Non-HDL cholesterol (mmol/L)	3.0 (0.8)	
< 2.5		10,138 (28.9)
≥ 2.5		24,838 (70.7)
Unknown		133 (0.4)
Presence of diabetic retinopathy		
Non-proliferative		12,618 (35.9)
Proliferative		159 (0.5)
No		21,372 (60.9)
Unknown		960 (2.7)
Presence of peripheral neuropathy		
Yes		3414 (9.7)
No		30,995 (88.3)
Unknown		700 (2.0)
Presence peripheral vascular disease		
Yes		54 (0.1)
No		34,719 (98.9)
Unknown		336 (1.0)

BP blood pressure, *HbA1c* glycated hemoglobin A1c, *Non-HDL* non-high density lipoprotein

34.1%) although their prevalence of albuminuria was a bit lower (15.4% and 19.5%) [33, 34].

The results of the NEFRON study demonstrated a relatively high prevalence of diabetic nephropathy in patients with type 2 diabetes in the setting of Australian primary care. The rates of diabetic nephropathy, albuminuria and impaired eGFR were found to be 47.1%, 34.6% and 23.1% respectively [35]. The higher prevalence might be attributed to a higher mean HbA1c level (mean HbA1c 7.4% (57 mmol/mol) vs 7.0% (53 mmol/mol) in our study population), more patients (80%) were smokers or ex-smokers, different patients' ethnicity and using MDRD study equation for estimating the GFR in the study.

A significant proportion of patients with type 2 diabetes was found to have diabetic nephropathy in our study. As discussed, both impaired GFR and albuminuria are independently associated with ESRF and all-cause and cardiovascular mortality [9, 10]. Although there was relatively small proportion of patients (1.2%) had severe chronic kidney disease with eGFR <30 ml/min/1.73 m^2, as compared to 6.3% and 8.4% in the studies performed in Spain and a Mediterranean area [33, 34], it could still cause a significant increase in the burden to our health care system with the rising prevalence of diabetes. Therefore, early recognition of the condition and control of the modifiable factors are of upmost importance in primary care.

A substantial proportion of patients in our study had hypertension. Our study supported the well-known fact that hypertension and suboptimal BP control are independent risk factors for diabetic nephropathy [25–28]. Suboptimal glycemic control and longer duration of diabetes were also factors associated with diabetic nephropathy [25–28]. Tight blood glucose control targeting at HbA1c less than 7% (53 mmol/mol) is important to prevent the development of microalbuminuria and delay the progression to overt nephropathy [27]. Suboptimal control of non-HDL cholesterol

Table 2 Prevalence of diabetic nephropathy, albuminuria and impaired eGFR

No. of patients			
eGFR Categories (ml/min/1.73 m^2)	With albuminuria	Without albuminuria	Total no. of patients (%)
1 (≥ 90)	1833*	10,797	12,630 (36.0%)
2 (60–89)	3327*	13,226	16,553 (47.1%)
3 (30–59)	2277*	3228*	5505 (15.7%)
4 (15–29)	266*	109*	375 (1.1%)
5 (< 15)	31*	15*	46 (0.1%)
Total	7734 (22.0%)	27,375 (78.0%)	35,109 (100.0%)

No. of patient with eGFR <60 ml/min/1.73m^2 : 5926 (16.9%)

eGFR estimated glomerular filtration rate

*No of patients with diabetic nephropathy: 11086 (31.6%)

was also associated with diabetic nephropathy as shown by our study and Toth [29]. This supported the need for achieving cholesterol goals as well in order to most optimally reduce the risk of diabetic nephropathy.

In keeping with the results of the study by Ravid et al., male sex, obesity and smoking were all significantly associated with diabetic nephropathy [26]. The other diabetic complications including diabetic retinopathy, peripheral neuropathy, peripheral vascular disease and history of stroke and ischemic heart disease were also demonstrated to have association with diabetic nephropathy in our study. Thus, screening and managing those modifiable factors in patients with type 2 diabetes is important in primary care before the development of microvascular and macrovascular complications.

The ADVANCE trial reported patients with type 2 diabetes who had moderate alcohol drinking had less microvascular

Table 3 Factors associated with diabetic nephropathy ($N = 32,375$)

Associated factors	Odd ratio (OR)	95% confidence interval (CI)	*p* value
Age	1.06	1.06–1.06	< 0.001
Male	1.27	1.19–1.35	< 0.001
Smoking			
Ex-smoker	1.20	1.11–1.29	< 0.001
Smoker	1.49	1.35–1.64	< 0.001
Drinking			
Social drinker	0.89	0.82–0.96	0.002
Drinker	0.72	0.61–0.85	< 0.001
Duration of diabetes	1.03	1.02–1.03	< 0.001
Hypertension	1.99	1.84–2.16	< 0.001
History of ischemic heart disease	1.22	1.11–1.35	< 0.001
History of stroke	1.50	1.35–1.66	< 0.001
BP ≥ 130/80 mmHg	1.26	1.20–1.33	< 0.001
Body mass index			
Overweight	1.08	1.00–1.17	0.043
Obesity	1.51	1.41–1.61	< 0.001
HbA1c ≥ 7% (53 mmol/mol)	1.28	1.21–1.35	< 0.001
Non-HDL cholesterol ≥2.5 mmol/L	1.20	1.13–1.27	< 0.001
Diabetic retinopathy			
Non-proliferative	1.47	1.40–1.55	< 0.001
Proliferative	6.52	4.53–9.36	< 0.001
Peripheral neuropathy	1.48	1.36–1.61	< 0.001
Peripheral vascular disease	2.19	1.12–4.29	0.023

BP blood pressure; *HbA1c* glycated hemoglobin A1c, *non-HDL* non-high density lipoprotein

complications including nephropathy than non-drinkers [30]. Our study showed a compatible finding with negative association between social or current drinking and diabetic nephropathy. The possible beneficial association might be explained by an anti-atherosclerotic effect with moderate alcohol consumption through increased HDL cholesterol and improved insulin sensitivity [36].

Limitations

There were several limitations in this study. Firstly, the cross-sectional design of our study limited the establishment of causal relationship between diabetic nephropathy and the associated risk factors. To determine their causal relationship, future longitudinal studies are needed. Secondly, only a single reading of urine ACR and estimation of GFR were used to determine the presence of albuminuria and diabetic nephropathy. Thus, we could not differentiate individuals with persistent elevation of urine ACR or impairment of eGFR and those with transient abnormality caused by some reversible conditions such as urinary tract infection, febrile illness, nephrolithiasis or drugs. Ideally, repeating the measurements at 3 months to confirm the diagnosis would be recommended. Thirdly, we did not take into consideration the use of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) and their effects when evaluating the associated factors for diabetic nephropathy. As recommended by international guidelines, they are the first line anti-hypertensive medications for patients with diabetes and we expected that most of our patients were taking ACEI or ARB. Therefore, the prevalence of diabetic nephropathy might be underestimated with the microalbuminuria detected in some patients reversed by treatment with ACEI or ARB. Finally, a small number of patients who were managed in our primary care clinics for diabetes but did not undergo the diabetic complication assessment program during the study period were not included in our study. Patients with missing creatinine or urinary ACR measurement were also excluded. These patients might have poorer treatment compliance leading to less optimal control of blood pressure, diabetes and hyperlipidemia. As a result, there could be underestimation of the prevalence of diabetic nephropathy in our study. On the other hand, overestimation of the prevalence might be due to impaired eGFR or albuminuria caused by other diseases including congenital kidney diseases, obstructive nephropathy or glomerulonephritis.

Conclusion

Our study demonstrated that diabetic nephropathy was a highly prevalent complication among Chinese patients with type 2 diabetes in primary care in Hong Kong. Age, male sex, longer duration of diabetes, obesity, smoking, hypertension, suboptimal control of blood pressure, HbA1c and non-HDL cholesterol, presence of diabetic complications including diabetic retinopathy, peripheral neuropathy and peripheral vascular disease and history of stroke and ischemic heart disease were all shown to have significant association with diabetic nephropathy. Strategies to recognize diabetic nephropathy and the associated risk factors and control the modifiable factors at early stages are warranted to prevent or delay the progression of diabetic nephropathy.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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