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The prevalence of microalbuminuria among patients with type II diabetes mellitus in a primary care setting: cross-sectional study

初級醫療機構裏乙型糖尿病患者出現微量蛋白尿的普遍程度：橫斷面研究

Objectives. To determine the prevalence of microalbuminuria among patients with type II diabetes mellitus in a primary care setting, and to study the association between various risk factors and the presence of microalbuminuria.
Design. Cross-sectional community-based study.
Setting. Four primary care clinics, Hong Kong.
Patients. All patients with type II diabetes mellitus who regularly attended the clinics between May 2002 and March 2003.
Main outcome measures. Patients' demographic data, the proportion with microalbuminuria (measured using a spot urine test), and the association between this condition and risk factors for diabetic nephropathy (via correlation and multivariable logistic regression analysis).
Results. The mean age of the 1161 patients in the sample population was 58.0 years. The mean duration of diabetes mellitus was 5.7 years, and the mean level of glycated haemoglobin was 7.4%. A total of 13.4% of the patients had microalbuminuria. Having the condition was significantly associated with advanced age, female sex, poor glycaemic control, and coexisting hypertension in both correlation and regression analyses. No significant association with ever smoking was found.
Conclusion. Early screening for incipient diabetic nephropathy and aggressive management of modifiable risk factors in a primary care setting may be important in optimising the renal outcome of patients with type II diabetes mellitus.

目的：檢定初級醫療機構裏乙型糖尿病患者出現微量蛋白尿的普遍程度，並探討各種風險因素與出現微量蛋白尿的相關性。
設計：社區性橫斷面研究。
安排：四家初級保健診所，香港。
病者：2002 年 5 月至 2003 年 3 月期間，所有往診所定期覆診的乙型糖尿病患者。
主要結果測量：患者的人口數據、患者出現微量蛋白尿的比例(以尿液樣本測試檢定)，以及通過相關和邏輯數據分析，探究微量蛋白尿與造成糖尿病腎病的風險因素之間的相關程度。
結果：研究樣本合共 1161 位患者，平均年齡 58.0 歲，患糖尿病平均 5.7 年，糖化血紅蛋白水平平均為 7.4%。13.4%的患者出現微量蛋白尿。結果亦顯示微量蛋白尿與多種因素息息相關，這些因素包括高齡、女性、血糖控制欠佳，以及同時出現的高血壓等，但跟長期吸煙的情況相關不大。
結論：在初級醫療機構裏，如能盡早替病人檢測是否患上早期糖尿病腎病，並積極抑制種種風險因素，這對提升乙型糖尿病患者的腎臟治療效果，是非常重要的。

Key words:
Diabetes mellitus, type II;
Diabetic nephropathies;
Hemoglobin A, glycosylated;
Prevalence

關鍵詞：
糖尿病，乙型；
糖尿病腎病；
A 型血紅蛋白，糖化；
普遍程度

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Introduction

With the growing prevalence of diabetes mellitus (DM), particularly type II DM, diabetic nephropathy has become the leading cause of end-stage renal disease worldwide.[1,2] In Hong Kong, diabetic nephropathy accounts for 30% to 40% of

Table 1. Patients' characteristics*

Characteristic	Male	Female	Total	P value
Patients	713 (61.4)	448 (38.6)	1161 (100.0)	-
Mean age (SD) [years]	57.2 (20.1)	59.2 (22.5)	58.0 (21.2)	0.002
Mean duration of diabetes mellitus (years)	5.5	6.0	5.7	0.064
Mean level of glycated haemoglobin (SD) [%]	7.3 (2.7)	7.5 (2.8)	7.4 (2.7)	0.029
Smoking status				
Non-smoker	538 (46.3)	432 (37.2)	970 (83.5)	-
Current smoker	83 (7.1)	7 (0.6)	90 (7.8)	<0.001
Ex-smoker	92 (7.9)	9 (0.8)	101 (8.7)	-
Presence of hypertension	324 (27.9)	259 (22.3)	583 (50.2)	<0.001
Presence of diabetic retinopathy	50 (4.3)	43 (3.7)	93 (8.0)	0.114

* Results are no. (%) unless otherwise stated

patients receiving renal dialysis—a larger proportion than that of patients receiving dialysis because of glomerulonephritis or hypertension.[3] Microalbuminuria, defined as a urinary albumin excretion rate of 30 to 300 mg/d, or 20 to 200 μg/min, is the earliest clinical sign of nephropathy.[4-7] Microalbuminuria is also regarded as a hallmark of the reversible stage of nephropathy, when appropriate and timely interventions can be instituted.[6] Without treatment, 20% to 40% of cases at this stage of disease would progress to overt nephropathy and by 20 years after the onset of overt nephropathy, at least 20% would develop end-stage renal disease.[7]

Besides being a predictor of incipient nephropathy, microalbuminuria is also a marker of greatly increased cardiovascular morbidity and mortality in patients with type I or type II DM. Microalbuminuria is thus an indicator of possible vascular disease requiring aggressive intervention to reduce cardiovascular risk.[7] Various epidemiological and cross-sectional studies have reported marked variation in the prevalence of microalbuminuria, ranging from less than 10% in the United Kingdom[8,9] to 18% in Singapore[10] and more than 30% in southern India.[11,12] In Hong Kong, the prevalence of microalbuminuria in nephrology units has been reported to be 15% to 18%.[6,13] Comparable data are missing from community-based centres, which in fact manage the majority of the patients with DM. These patients would probably experience the greatest benefit from appropriate interventions if instituted promptly. Thus, our study aimed at examining the prevalence of microalbuminuria among patients with type II DM in four primary care clinics in Hong Kong and at analysing the associations between different risk factors and the presence of the condition. This information would enable physicians to determine the treatment focus more effectively.

Methods

We conducted a cross-sectional community-based study that included all patients with type II DM who regularly attended the four primary care clinics in Hong Kong (the Family Medicine Training Centre in Ngautaukok and the three family clinics in Yaumatei, Wanchai, and Chai Wan) between May 2002 and March 2003. The majority of patients were diagnosed as having type II DM at these clinics according to the criteria proposed by the American Diabetes Association and WHO.[14] Others had been referred to the clinics either from public hospitals or from other primary care clinics because of geographical reasons or patients' preferences. All patients were entered into a computerised DM-microalbuminuria registry, in which data including age, sex, date of diagnosis of DM, duration of DM, smoking status, history of hypertension, most recent level of glycated haemoglobin (HbA_{1c}), diabetic retinopathy status, and extent of microalbuminuria were recorded and regularly updated by nurses during each follow-up visit.

Table 2. Clinitek 50 test results, by sex*

Test result	Male	Female	**Total**
Negative (<30 mg/g)	638 (55.0)	367 (31.6)	1005 (86.6)
Positive (≥30 mg/g)	75 (6.5)	81 (7.0)	156 (13.4)

* Results are no. (%)

The smoking status options were non-smoker, current smoker, and ex-smoker (which was defined as having completely quitted for at least 6 months consecutively). Hypertension was defined as having a blood pressure that was persistently above 130/80 mm Hg or as receiving any antihypertensive drug. The diagnosis of diabetic retinopathy was based on yearly fundus photography or an ophthalmologist's opinion. The patients were then tested for microalbuminuria using Clinitek 50 (Bayer Diagnostic Manufacturing Ltd, Bridgend, United Kingdom), which is a semiquantitative screening tool that measured the albumin-to-creatinine ratio from a spot urine specimen. In this study, the microalbuminuria test result was regarded as positive if the albumin-to-creatinine ratio was at least 30 mg/g, and as negative if it was less than 30 mg/g. Patients who had a positive result to the Albustix test (Bayer Diagnostic Manufacturing Ltd, Bridgend, United Kingdom), other renal pathology (eg urinary tract infection), haematuria, acute febrile illness, or congestive heart failure were excluded from Clinitek 50 testing.

Of the 1262 patients who were eligible for microalbuminuria testing, 101 (8.0%) were excluded from statistical analysis because of missing data. Data from a total of 1161 patients were thus analysed using the Statistical Package for the Social Sciences version 10.0 (SPSS Inc,

Table 3. Patients' characteristics, by Clinitek 50 test results*

Characteristic	Clinitek 50–negative	Clinitek 50–positive	P value	*r* value
Mean age (SD) [years]	57.5 (20.9)	61.3 (21.6)	0.002	0.118
Sex				
Male	638 (55.0)	75 (6.5)	-	-
Female	367 (31.6)	81 (7.0)	<0.001	0.107
Mean duration of diabetes mellitus (years)	5.6	6.7	0.007	0.102
Mean level of glycated haemoglobin (SD) [%]	7.3 (2.7)	7.7 (2.7)	0.021	0.112
Smoking status				
Non-smoker	832 (71.7)	138 (11.9)	-	-
Current smoker	79 (6.8)	11 (0.9)	0.116	0.061
Ex-smoker	94 (8.1)	7 (0.6)	-	-
Presence of hypertension	476 (41.0)	107 (9.2)	<0.001	0.143
Presence of diabetic retinopathy	74 (6.4)	19 (1.6)	0.039	0.060

* Results are no. (%) unless otherwise stated

Chicago [IL], United States). The Chi squared test was used to compare categorical variables, and the Mann-Whitney *U* test was used to analyse continuous variables because the data were not normally distributed. The correlation between variables was assessed by calculating the contingency coefficients. Furthermore, multivariable logistic regression was performed to delineate the association between independent variables and the presence of microalbuminuria, using the cut-off value of significance of P<0.05.

Results

Patients' ages ranged from 18.0 to 81.0 years (mean age, 58.0 years) [Table 1]. The mean duration of DM was 5.7 years and the mean HbA_{1c} level was 7.4%. More than half of the patients were hypertensive. Some 7.8% currently smoked and another 8.0% had diabetic retinopathy. Compared with the men, women were older (P=0.002) and had a higher mean HbA_{1c} level (P=0.029). Nevertheless, results also show a significantly larger proportion of men than women currently smoked (P<0.001) and were hypertensive (P<0.001). There were no significant differences between men and women with regard to the duration of DM (P=0.064) and diabetic retinopathy (P=0.114).

The prevalence of microalbuminuria among our sample was 13.4% (Table 2). Microalbuminuria in patients with DM was positively associated with advanced age, female sex, poor glycaemic control, long duration of DM, diabetic retinopathy, and coexisting hypertension in correlation analysis (Table 3). Women were older than men and had poorer diabetic control; however, the association was still significant after adjustment for age and HbA_{1c} level (Table 4). We did not find a significant association between microalbuminuria and smoking, in either the correlation or regression tests.

Discussion

The subject of microalbuminuria has attracted much clinical attention in recent years, because the condition is much more important than its name implies: it is a predictor of advanced nephropathy,[4,6,7,12,15,16] a risk indicator of cardiovascular death,[7,12] a key feature in the metabolic syndrome,[7,12,17] and even a marker of increased overall mortality.[4,15,18] Furthermore, this stage of incipient nephropathy is potentially salvageable if detected early and if targeted interventions are implemented.[19-21]

Table 4. Results of multivariable logistic regression assessing the association between selected variables and presence of microalbuminuria

Variable	Odds ratios	95% CI*	P value
Mean age (years)	1.021	1.003-1.039	0.02
Male sex†	0.673	0.468-0.970	0.034
Mean duration of diabetes mellitus	1.012	0.980-1.045	0.479
Mean level of glycated haemoglobin (%)	1.185	1.051-1.335	0.005
Ever smoked‡	1.477	0.850-2.568	0.167
Absence of hypertension§	0.483	0.331-0.704	<0.001

* Confidence interval
† Reference group: female sex
‡ Reference group: never smoked
§ Reference group: presence of hypertension

With a cut-off point of 30 mg/L, the Clinitek 50 test kit has a sensitivity of 97%, specificity of 83%, positive predictive value of 73%, and negative predictive value of 98%, thereby allowing detection or exclusion of microalbuminuria.[22] It is also non-expensive and easy to use, and it has been verified by local authorities to be superior to the other commercial techniques available and the 24-hour or timed urinalysis as a large-scale screening test.[6]

The prevalence of microalbuminuria in this study, of 13.4%, is just below that reported by tertiary centres in Hong Kong (18%, which is also based on the Clinitek 50 test).[6] In concordance with many international studies,[9,12,15-17] we have also demonstrated the strong association of microalbuminuria with age, glycaemic control, hypertension, and the presence of retinopathy. We cannot overemphasise the importance of optimal glycaemic and blood pressure control in the prevention of diabetic nephropathy.

The Diabetes Control and Complications Trial and the

United Kingdom Prospective Diabetes Study have shown definitively that intensive DM therapy can significantly reduce the risk of development of microalbuminuria and overt nephropathy in people with DM.[7] Antihypertensive treatment to maintain a blood pressure below 130/80 mm Hg may also slow the progression of diabetic renal disease, reduce the need for dialysis and transplantation, and lower the overall mortality.[4,7] Regression of microalbuminuria may even be possible in type I DM with salutary levels of glycated haemoglobin (<8%), low systolic blood pressure (<115 mm Hg), and low levels of cholesterol and triglycerides (<5.12 mmol/L and 1.64 mmol/L, respectively).[23]

As illustrated in this and many other pieces of research, diabetic retinopathy often accompanies nephropathy. Some researchers have also suggested a corresponding increase in neuropathy.[24] In contrast to other reports,[25,26] however, this study does not show a clear risk of smoking in diabetic nephropathy. The hazardous effect of smoking may be blurred by the substantially lower proportion of smokers (7.8%) in our patient sample than that in the western studies (14%-28%).[17] Concerning the difference in risk of microalbuminuria by sex, there is still a lack of consensus across different studies.[27-32] Notably, we found that female sex was independently associated with the development of microalbuminuria.

Our study has some limitations. Firstly, because the three family clinics exclusively serve civil servants who might be more health-conscious than the general public and have more ready access to the health care system, the results may not represent the primary care population as a whole. Secondly, collecting a spot urine sample for microalbuminuria testing is technically more feasible but is less sensitive than collecting an early-morning urine specimen. Thirdly, the missing data, although very few, may affect the statistical analysis. Finally, some other major cardiovascular risk factors, such as hyperlipidaemia and obesity, were not covered here; however, they are covered by ongoing studies that investigate the clinical progress of the microalbuminuria cohort, stratified by duration of DM, glycaemic control, diabetic retinopathy, and treatment with angiotensin-converting enzyme inhibitor.

Conclusion

The prevalence of microalbuminuria in type II DM among patients in our study is 13.4%. According to ancient medical wisdom, an ounce of prevention is worth a pound of cure. To optimise the renal outcome of patients with DM, effective screening of microalbuminuria in a primary care setting, at least for the high-risk group, is important; so is the active management of modifiable risk factors—in particular, hyperglycaemia and hypertension.

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References

1. Cordonnier D, Bayle F, Benhamou PY, et al. Future trends of management of renal failure in diabetics. Kidney Int Suppl 1993;41 (Suppl):8S-13S.
2. Ritz E, Stefanski A. Diabetic nephropathy in type II diabetes. Am J Kidney Dis 1996;27:167-94.
3. Lui SF, Ho YW, Chau KF, Leung CB, Choy BY. Hong Kong renal registry 1995-1999. Hong Kong J Nephrol 1999;1:53-60.
4. Mogensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. N Eng J Med 1984; 310:356-60.
5. Nelson RG, Knowler WC, Pettitt DJ, Saad MF, Charles MA, Bennett PH. Assessment of risk of overt nephropathy in diabetic patients from albumin excretion in untimed urine specimens. Arch Intern Med 1991;151:1761-5.
6. Wong KY, Lam MF, Leung YH, et al. Detection of microalbuminuria in non–insulin-dependent diabetes mellitus (NIDDM) patients without overt proteinuria by a semiquantitative albumin-creatinine urine strips. Hong Kong Journal of Nephrology 1999;1:18-22.
7. American Diabetes Association. Diabetic nephropathy. Diabetes Care 2002;25(Suppl 1): 85S-89S.
8. Gatling W, Knight C, Mullee MA, Hill RD. Microalbuminuria in diabetes: a population study of the prevalence and an assessment of three screening tests. Diabet Med 1988;5:343-7.
9. Marshall SM, Alberti KG. Comparison of the prevalence and associated features of abnormal albumin excretion in insulin-dependent and non–insulin-dependent diabetes. Q J Med 1989; 70:61-71.
10. Leong SO, Lui KF, Ng WY, Thai AC. The use of semi-quantitative urine test-strip (Micral Test) for microalbuminuria screening in patients with diabetes mellitus. Singapore Med J 1998;39:101-3.
11. Hamman RF, Franklin GA, Mayer EJ, et al. Microvascular complications of NIDDM in Hispanics and non-Hispanic whites. San Luis Valley Diabetes Study. Diabetes Care 1991;14:655-64.
12. Varghese A, Deepa R, Rema M, Mohan V. Prevalence of microalbuminuria in type 2 diabetes mellitus at a diabetes centre in southern India. Postgrad Med J 2001;77:399-402.
13. Tiu SC, Lee SS, Cheng MW. Comparison of six commercial techniques in the measurement of microalbuminuria in diabetic patients. Diabetes Care 1993;16:616-20.
14. Chan CN, Yeung TF, Chow CC, Ko TC, Cockram CS. A manual for management of diabetes mellitus: a Hong Kong Chinese perspective. Hong Kong: The Chinese University Press; 1998:16.
15. Erasmus RT, Oyeyinka G, Arije A. Microalbuminuria in non–insulin-dependent (type 2) Nigerian diabetics: relation to glycaemic control, blood pressure and retinopathy. Postgrad Med J 1992; 68:638-42.
16. Mather HM, Chaturvedi N, Kehely AM. Comparison of prevalence and risk factors for microalbuminuria in South Asians and Europeans with type 2 diabetes mellitus. Diabet Med 1998;15:672-7.
17. Niskanen LK, Pentilla I, Parviainen M, Uusitupa MI. Evolution, risk factors, and prognostic implications of albuminuria in NIDDM. Diabetes Care 1996;19:486-93.
18. Jarrett RJ, Viberti GC, Argyropoulos A, Hill RD, Mahmud U, Murrells TJ. Microalbuminuria predicts mortality in non-insulin-dependent diabetics. Diabet Med 1984;1:17-9.
19. Mathiesen ER, Hommel E, Giese J, Parving HH. Efficacy of captopril in postponing nephropathy in normotensive insulin dependent dia betic patients with microalbuminuria. BMJ 1991;303:81-7.
20. Comparison between perindopril and nifedipine in hypertensive and normotensive diabetic patients with microalbuminuria. Melbourne Diabetic Nephropathy Study Group. BMJ 1991;302:210-6.

21. Cooper ME. Renal protection and angiotensin-converting enzyme inhibition in microalbuminuric type I and type II diabetic patients. J Hypertens 1996;14(Suppl):11S-14S.
22. Kutter D. A chemical test strip to determine low concentration of albumin and creatinine in urine. Lab Med 1998;29:769-72.
23. Perkins BA, Ficociello LH, Silva KH, Finkelstein DM, Warram JH, Krolewski AS. Regression of microalbuminuria in type 1 diabetes. N Eng J Med 2003;348:2285-93.
24. Partanen J, Niskanen L, Lehtinen J, Mervaala E, Siitonen O, Uusitupa M. Natural history of peripheral neuropathy in non–insulin-dependent diabetes mellitus. N Eng J Med 1995;333:89-94.
25. Sawicki PT, Didjurgeit U, Muhlhauser I, Bender R, Heinemann L, Berger M. Smoking is associated with progression of diabetic nephropathy. Diabetes Care 1994;17:126-31.
26. Ritz E, Tarng DC. Renal disease in type 2 diabetes. Nephrol Dial Transplant 2001;16(Suppl 5):11-8.
27. Seliger SL, Davis C, Stehman-Breen C. Gender and the progression of renal disease. Curr Opin Nephrol Hypertens 2001;10:219-25.
28. Neugarten J, Acharya A, Silbiger SR. Effect of gender on the progression of nondiabetic renal disease: a meta-analysis. J Am Soc Nephrol 2000;11:319-29.
29. Silbiger SR, Neugarten J. The impact of gender on the progression of chronic renal disease. Am J Kidney Dis 1995;25:515-33.
30. Li PK, Ho KK, Szeto CC, Yu L, Lai FM. Prognostic indicators of IgA nephropathy in the Chinese—clinical and pathological perspectives. Nephrol Dial Transplant 2002;17:64-9.
31. Coggins CH, Breyer Lewis J, Caggiula AW, Castaldo LS, Klahr S, Wang SR. Differences between women and men with chronic renal disease. Nephrol Dial Transplant 1998;13:1430-7.
32. Jafar TH, Schmid CH, Stark PC, et al. The rate of progression of renal disease may not be slower in women compared with men: a patient-level meta-analysis. Nephrol Dial Transplant 2003;18:2047-53.