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Original Article

Justifying the high prevalence of microalbuminuria for type 2 diabetic patients in Taiwan with conditional probability approach—a DEMAND II Study ☆

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Abstract

Background: To examine the prevalence of microalbuminuria (MAU) and chronic kidney disease as well as the correlation between MAU and renal and cardiovascular risks of Type 2 diabetes mellitus (T2DM) patients for public health policy making in Taiwan.
Methods: This was a multicenter, hospital-based, randomly selected, and cross-sectional study. T2DM patients aged 18−80 years without a known diagnosis of proteinuria were eligible. MAU was defined as urinary albumin-to-creatinine ratio (ACR) within 30−299 mg/g, and macroalbuminuria as that greater than or equal to 300 mg/g. Two positive out of three urinary screening results were required to make the diagnosis of MAU. The adjusted prevalence of MAU was calculated by conditional probability approach.
Results: 51.1% of the analyzed population ($n = 1,827$) were women, with a mean (standard deviation) age of 59.16 years (11.19 years) and mean hemoglobin A1c (HbA1c) of 8.15% (1.83%). Median duration of DM history was 6 years (interquartile range, 3−11 years). The adjusted prevalence of MAU was 26.9%. Overall prevalence of chronic kidney disease Stage 3 or higher (estimated Glomerular filtration rate (eGFR) less than 60/mL/min/1.73 m^2) was 13.8%. Only 4.7% of the T2DM patients had serum albumin test recorded and 68.7% with serum creatinine test recorded within the last 6 months. After adjustment for center and gender, the odds ratios for MAU or macroalbuminuria were 1.73 (95% CI,

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1.27−2.36) for age greater than or equal to 60 years, 1.54 (1.13−2.10) for abnormal waist circumference, 1.10 (1.02−1.19) for every 1% increase in hemoglobin A1c, 1.91 (1.38−2.65) for higher systolic blood pressure, and 1.92 (1.19−3.07) for abnormal serum creatinine level. *Conclusion*: This study demonstrates the application of "conditional probability" method to justify the rationale of adopting two positive out of three urinary screening tests for the diagnosis of MAU. An adjusted prevalence rate of MAU as 26.9% is reported. These results may provide a basis for cost−benefit consideration in designing preventive and interventional policies in public health. Furthermore, the awareness and practice of early monitoring of MAU for DM patients should be strengthened.

Keywords: Chronic kidney disease; Conditional probability; Microalbuminuria; Taiwan; Type 2 diabetes

1. Introduction

Microalbuminuria (MAU) has been reported as an important risk factor for the progression of renal and cardiovascular diseases in diabetes mellitus (DM) patients since 1974.[1,2] In 2003, the guidelines of the American Diabetes Association (ADA) recommended annual screening of MAU to be performed in diabetic patients.[3] The Chinese Taipei Diabetes Association[4] also announced its recommendation to adopt ADA standards. High prevalence of MAU in Type 2 DM (T2DM) patients has been reported in Asia. According to the Microalbuminuria Asian Prevalence Study, the prevalence of MAU was reported as 39.8% and macroalbuminuria as 18.8% in Asian population. In this survey, around 40% of the patients screened in Taiwan had MAU.[5] The Developing Education on MAU for Awareness of reNal and cardiovascular risk in Diabetes (DEMAND) Study reported similar prevalences (43% for MAU and 12% for proteinuria) in Asia and approximately 61.7% for MAU in Taiwanese population,[2] which seemed to be the highest in the region. Therapeutic intervention has proven to be effective in slowing the progression to overt nephropathy.[6] It is, therefore, critically important to identify kidney disease at the earliest stage to delay the evolution to overt nephropathy and its subsequent risk of end-stage renal disease, particularly in T2DM patients.

The main objective of this study was to further confirm the prevalence of MAU in Taiwan and to evaluate the correlation between MAU and other well-known renal and cardiovascular risk factors. Through the understanding of the local disease community, it is our ultimate goal to increase physician awareness, by medical education, on the importance of annual urinary albumin screening in T2DM patients to improve patients' quality of care and make public health policy in Taiwan.

2. Methods

2.1. Patients and study design

T2DM patients who visited outpatient clinics in the 11 participating tertiary medical centers in Taiwan were the target of the survey population. Random tables with selecting marks were provided to all participating hospitals, and two out of every 10 sequential T2DM patients were randomly selected from each physician's clinic.

The inclusion criteria for the selected T2DM patients were age between 18 and 80 years and no known diagnosis of proteinuria or acute fever. Female patients who were pregnant or in menstruation period were excluded.

Three urine screening tests were performed within 6 months after inclusion. At the first screening visit, demographic and the following information were collected from the medical records: DM, hypertension and cardiovascular disease history, drug treatment records, and biochemical laboratory data in the last 6 months before the first visit date.

The major process of urine screening was as follows. In the beginning, every patient took the first urine screening; if the result from the first screening was positive for MAU or macroalbuminuria, a second follow-up screening should be done within the coming 3 months. Unless the second result was also positive, the third follow-up screening should again be done within the next 3 months from the second visit date (Fig. 1). Two additional processes were designed to provide further information for conditional probability approach. One process was that patients completed the first and second screenings within 3 months from the date of first visit; if the results from these two screenings were different and could not determine the final MAU status, then a third follow-up screening should be done within the next 3 months. Two centers executed this process. The other process was that each patient had to complete all the three urinary screenings. One center executed the last kind of process. The diagnosis of MAU was defined as two positive out of three urinary screening results.

2.2. Assays

In each screening, a random urine specimen was used to measure albumin-to-creatinine ratio (ACR). The urine albumin and creatinine levels were tested by a commercial dipstick, Microalbustix (Microalbustix Bayer, Bridgend, UK). This test provided semi-quantitative results with 89% accuracy, 90% sensitivity, and 88% specificity for albumin, and 88% accuracy, 84% sensitivity, and 91% specificity for ACR (information

The 1st test	The 2nd test	The 3rd test	MAU Result
−	×	×	−
+	−	−	−
+	−	+	+
+	+	×	+

Fig. 1. The major process for urine sample screening. Note: × means that there is no follow-up urine test (missing).

provided by the Microalbustix Bayer). Urine specimens with creatinine level less than 10 mg/dL were considered as over-diluted and were tested twice. If both results were the same, 10 mg/dL for creatinine level was used to measure the ACR. MAU and macroalbuminuria were defined as having ACR within 30−299 mg/g and greater than or equal to 300 mg/g, respectively. Proteinuria was tested by Uristix (Bayer, Bridgend, UK). The accuracy, sensitivity, and specificity of ACR measurement by Microalbustix dipstick was verified using radioimmunoassay as standard on 11 patients. The results were 81.8%, 100%, and 60%, respectively.

2.3. Populations

The study was conducted from March 1, 2005, to February 9, 2006, with a total of 56 physicians from 11 medical centers participating. Out of 2,730 randomly selected patients, 1,924 were eligible for enrollment. The survey protocol was approved by the Joint Institutional Review Board in Taiwan,[7] and informed consent was obtained from each patient. The screening failure rate was 29.5%: 11.0% because of known or new diagnosis of proteinuria, 2.3% for age violation, 11.9% for patient disagreement, and 4.3% for other reasons. In detail, out of 1,924 eligible participants, 1,111 patients had only the first urine test result, 574 had both the first and second test results, and 239 had all the three urine test results. Ninety-seven patients were lost to follow-up, which makes a total per-protocol analyzed population of 1,827 patients. Figure 2 illustrates the patient enrollment status.

2.4. Statistical methods

Population characteristics were summarized into mean, standard deviation (SD), or median for quantitative variables and count, percentage for categorical data. The crude prevalences of MAU and macroalbuminuria were reported globally. The final prevalence of MAU was provided by the conditional probability approach for missing adjustment. Student's *t*-test was used to compare quantitative variables and Chi-squared test or Fisher's exact test for categorical variables. The Kaplan−Meier method was used to estimate the age and DM duration of the 25th-percentile or median MAU cumulative incidence. Multivariate logistic regression was used to evaluate the risk factors of MAU or macroalbuminuria. A p value less than 0.05 was considered statistically significant. All statistical analyses were performed by SAS version 9.0 (SAS Institute, Cary, NC, USA).

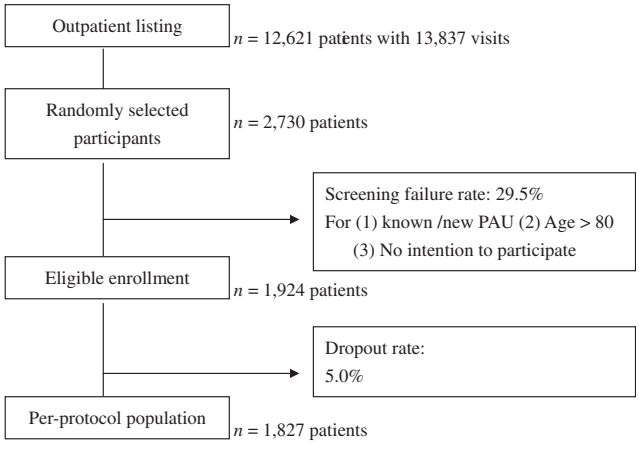

Fig. 2. Patient disposition and enrollment flow chart.

The principle of probability calculation under the conditional probability approach was similar to the serial screening test in disease screening. As Fig. 1 illustrates, when the first screen test was negative, there would be no second and third tests, and these patients were counted as "missing." By the additional two screening processes, the data of patients who completed at least two screening tests were used to estimate the probability of each possible outcome of the second screening, given the first screening result, and the data of patients who completed all the three screening tests were used to estimate the probability of each possible outcome of the third screening, given the first and second screening results. Then, the final outcome probability could be calculated by multiplying the third screening probability with the given condition probability. Finally, we added up the probabilities of all possible final outcomes that indicated the diagnosis of MAU as the so-called "the adjusted prevalence," as Table 1 demonstrates. The gray cells in Table 1 show that the probability, unreasonably affected by the sparse count of the third screening, had been corrected by contingency factor or the estimation from the second screening.

3. Results

3.1. Patient characteristics

Mean and SD of age were 59.16 years and 11.19 years, respectively. The odds for men and women were 48.9% versus 51.1%. The means (SD) for weight, waist circumference, and body mass index were 65.97 kg (12.1 kg), 87.95 cm (10.7 cm), and 25.65 kg/m^2 (4.1 kg/m^2), respectively. Mean (SD) of HbA1c was 8.15% (1.83%), systolic blood pressure (SBP) was 131.64 mmHg (17.0 mmHg), and diastolic blood pressure was 76.67 mmHg (10.9 mmHg). Median duration of DM history was 6 years, with interquartile range of 3−11 years.

3.2. Prevalence of MAU

The prevalence of MAU was 19.2% (351 out of 1,827), with a 95% confidence interval (CI) of 17.4−21.0%. The adjusted prevalence of MAU was 26.9% by conditional probability approach, as shown in Table 1. Based on these MAU results of 239 patients who completed three screening tests, the false-negative (FN) rate of the first screening test was found to be 5.84%, and the false-positive (FP) rate was found to be 65.7% (67 out of 102). By conditional probability approach, the FN rate rose to 6.87% and FP rate went down to 5.55%.

According to the classic epidemiological method, using the age structure of Taiwan population in December 2005 as standard, the age-adjusted prevalence was 11.1%. By Kaplan−Meier method, the age of 25th-percentile MAU

Table 1
The micro- and macroalbuminuria prevalence counted by conditional probability

First screening			Second screening			Third screening			Final outcome			
									Final[c]		Diagnosis	Total
Code[a]	Freq	Prob(f)	Code	Freq	Prob(s | f)	Code	Freq	Prob(t | f&s)	Code	Prob(f_s_t)[d]	Result	Probability
N(f)	1,924		N(s| f)[b]	345		N(t| f&s)	120					
0	1,396	0.7256	0	280	0.8116	0	112	0.9333	000	0.5496	Normo-AU	
						1	7	0.0583	001	0.0344	Normo-AU	
						2	1	0.0083	002	0.0049	Normo-AU	
						N(t| f&s)	15.5					Normo-AU
			1	61	0.1768	0	8	0.5161	010	0.0662	Normo-AU	0.7122
						1	7	0.4516	011	0.0579	Micro-AU	
						2	0.5	0.0323	012	0.0041	Micro-AU	
						N(t| f&s)	2					
			2	4	0.0116	0	1	0.2027	020	0.0017	Normo-AU	
						1	1	0.5270	021	0.0044	Micro-AU	
						2	0	0.2703	022	0.0023	Macro-AU	
			N(s| f)	393		N(t| f&s)	73					
1	446	0.2318	0	108	0.2748	0	56	0.7671	100	0.0489	Normo-AU	
						1	14	0.1918	101	0.0122	Micro-AU	
						2	3	0.0411	102	0.0026	Micro-AU	
						N(t| f&s)	13					Micro-AU
			1	262	0.6667	0	2	0.1538	110	0.0238	Micro-AU	0.2687
						1	7	0.5385	111	0.0832	Micro-AU	
						2	4	0.3077	112	0.0476	Micro-AU	
						N(t| f&s)	2					
			2	23	0.0585	0	1	0.2027	120	0.0027	Micro-AU	
						1	0	0.5270	121	0.0071	Micro-AU	
						2	1	0.2703	122	0.0037	Macro-AU	
			N(s| f)	74		N(t| f&s)	14.5					
2	82	0.0426	0	15	0.2027	0	11	0.7586	200	0.0066	Normo-AU	
						1	3	0.2069	201	0.0018	Micro-AU	
						2	0.5	0.0345	202	0.0003	Macro-AU	
						N(t| f&s)	0					Macro-AU
			1	39	0.5270	0	0	0.2748	210	0.0062	Micro-AU	0.0191
						1	0	0.6667	211	0.0150	Micro-AU	
						2	0	0.0585	212	0.0013	Macro-AU	
						N(t| f&s)	0					
			2	20	0.2703	0	0	0.2027	220	0.0023	Macro-AU	
						1	0	0.5270	221	0.0061	Macro-AU	
						2	0	0.2703	222	0.0031	Macro-AU	

The code f = the first, s = the second, and t = the third screening, e.g. Prob(s = 0|f = 0) = N(s = 0|f = 0)/N(s = 0,1,2 and f = 0) = 280/345 = 0.816.
Macro-AU = macroalbuminuria; Micro-AU = microalbuminuria; Normo-AU = normoalbuminuria.
The gray cells show that the probability, unreasonably affected by the sparse count of the third screening, had been corrected by contingency factor or the estimation from the second screening.

[a] Code value: 0 = normoalbuminuria, 1 = microalbuminuria, and 2 = macroalbuminuria.

[b] N(s| f) = the total frequency of all possible outcomes for the second test, given the specific outcome of the first test.

[c] Final code: 012 means the outcomes of the three screenings were normoalbuminuria for the first, microalbuminuria for the second, and macroalbuminuria for the third, and so forth.

[d] Prob(f_s_t) = Prob(t | f&s) × Prob(s | f) × Prob(f).

cumulative incidence was found to be 69 years. The DM duration of median MAU cumulative incidence was 23 years (Fig. 3A and B).

3.3. Risk factor evaluation

Table 2 compares the results of demographic variables between the MAU and normoalbuminuria groups. The MAU patients were older and had greater weight, larger waist circumference, higher body mass index, worse HbA1c control, and higher SBP.

MAU patients had a mean (SD) duration of 8.5 years (6.7 years) of DM history, longer than that of normoalbuminuria patients, and also had greater percentage of retinopathy complication (28.9% *vs.* 21.5%, $p = 0.003$). Concerning drug therapies, 82.2% of MAU patients were treated with oral antidiabetic agents, 9.2%, 7.5%, and 1.2% for insulin alone, oral antidiabetic agents plus insulin, and no drug

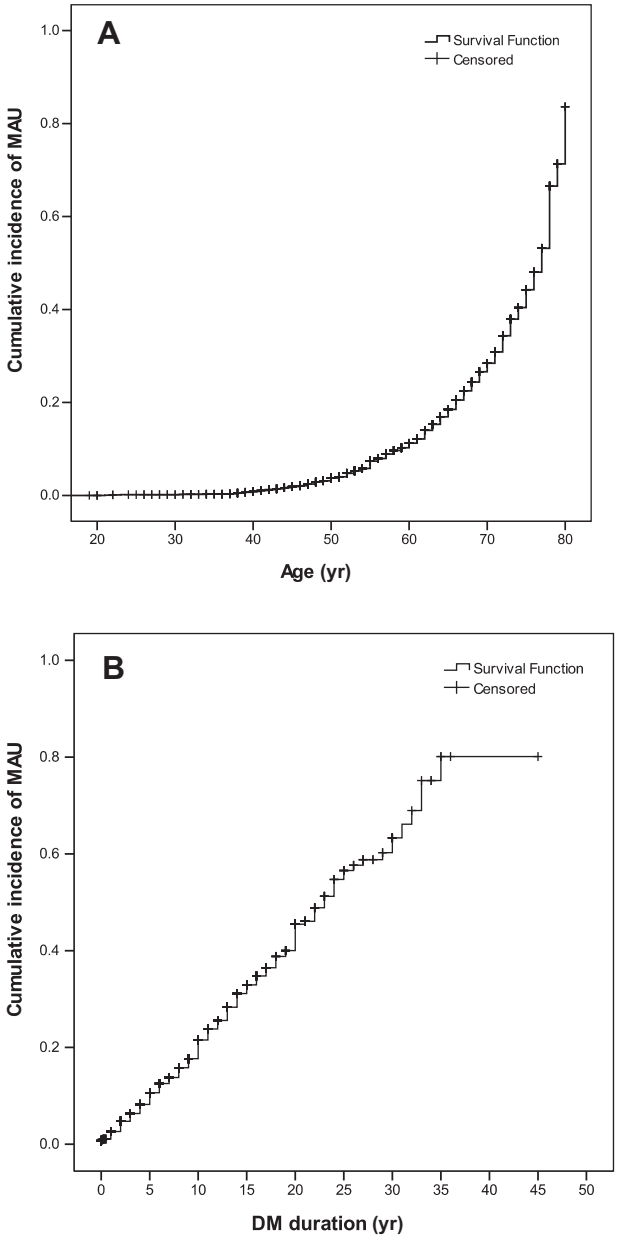

Fig. 3. (A) Cumulative incidence of microalbuminuria (MAU) plotted against age. (B) Cumulative incidence of microalbuminuria plotted against diabetes mellitus (DM) duration.

therapy, respectively, compared with 83.5%, 5.7%, 6.8%, and 4.1%, respectively, in normoalbuminuria patients ($p = 0.006$).

The T2DM patients with a history of hypertension were more likely to have MAU compared with those without hypertension (56% *vs.* 44%, $p = 0.004$). MAU patients had statistically significant higher SBP (134.5 mmHg *vs.*130.8 mmHg, $p < 0.001$). For those 951 (52.6%) T2DM patients with hypertension history, totally 816 (85.8%) received antihypertensive drug treatment: 59.2% patients had a single drug, 27.9% had two-drug combination, and 12.9% had three or more drug combination treatment; on average, 1.5 drugs were used per patient. Most of the prescriptions were for angiotensin receptor blockers (ARB) (39.0%), followed by calcium channel blockers (35.4%), angiotensin-converting enzyme (ACE) inhibitors (31.1%), beta blockers (22.7%), diuretics (21.7%), and alpha blockers (5.0%). Excluding three patients with ARB and ACE combined therapy, the association between MAU or macroalbuminuria and antihypertension drug (ACE only/combination *vs.* ARB only/combination *vs.* other drugs only/combination without ACE or ARB) was not statistically significant ($p = 0.614$). The percentages of MAU in the drug groups were 18.7%, 22.2%, and 23.48%, respectively.

Data on seven laboratory parameters measured in the latest 6 months before enrollment—blood urea nitrogen, creatinine, albumin, triglycerides, high-density-lipoprotein cholesterol, low-density-lipoprotein cholesterol, and uric acid—were recorded and evaluated for their possible association with MAU. Validity of laboratory data was highest for triglycerides (73.9%) and lowest for albumin (4.7%). Thus, among the MAU-related laboratory parameters, only 4.7% of the T2DM patients had serum albumin test recorded and 68.7% with serum creatinine test recorded within the latest 6 months. This information indicated relatively low awareness of chronic kidney disease (CKD) either in patients or physicians. Based on these limited data, MAU patients showed statistically significant mean difference from normoalbuminuria patients in terms of blood urea nitrogen, creatinine, high-density-lipoprotein cholesterol, and low-density-lipoprotein cholesterol (Table 2).

For the covariate-adjusted multivariate analysis, Table 3 presents the final result of multivariate logistic regression. As only 66.5% of the patients had serum creatinine measured, the effective sample size for Model 2 was lowered to 1,181. We found that the estimated odds ratios were very similar and consistent between these two models. The continuous variables were categorized for interpretation.

Based on Model 2, after adjustment for center, gender, and diastolic blood pressure, the patients older than 60 years had an odds ratio of 1.73 (95% CI, 1.26–2.36) of having MAU or macroalbuminuria compared with those who were younger than 60 years. The odds ratios (95% CIs) for MAU or macroalbuminuria were 1.1 (1.02–1.2) for every 1% HbA1c increase, 1.54 (1.13–2.10) for abnormal waist circumference, 1.91 (1.37–2.65) for higher SBP, and 1.92 (1.20–3.07) for abnormal serum creatinine level.

There were 13.7% (171 out of 1,246 patients with eligible data) of patients found with CKD Stage 3 or higher (estimated GFR less than 60/mL/min/1.73 m^2) in this study. Partitioned into normoalbuminuria, MAU, and macroalbuminuria, 11.2%, 22.4%, and 29.4% of patients, respectively, were found with CKD Stage 3 or higher. Patients with CKD Stage 3 or higher had a higher rate of MAU or macroalbuminuria (36.3%; 62 out of 171) compared with patients with CKD Stage less than 3 (19.4%; 209 out of 1,075)—$p < 0.001$.

4. Discussion

MAU prevalences reported in the DEMAND Study were 39% globally and 43% in Asia versus only 26.9% in our study, which used a more concise and conservative diagnostic definition. “Transient physiological proteinuria,” such as that after

Table 2
The comparison among micro-, macro-, and normoalbuminuria patients

	Total (n=1,827)	Normoalbuminuria (n=1,455)		Microalbuminuria (n=351)			Macroalbuminuria (n=21)		
	n	Mean	SD	Mean	SD	p[a]	Mean	SD	p[b]
Age (yr)	1,820	58.51	11.08	61.74	11.02	<0.0001	61.14	14.97	<0.0001
Gender	1,820								
Female	930	735 (50.8%)		180 (51.3%)		0.861	15 (71.43%)		0.169
Male	890	713 (49.2%)		171 (48.7%)			6 (28.57%)		
Height (cm)	1,824	160.25	8.75	160.38	8.86	0.214	157.1	8.78	0.136
Weight (kg)	1,825	65.64	11.73	67.67	13.28	0.009	60.63	10.32	0.002
Waist (cm)	1,816	87.60	10.49	89.45	11.29	0.005	87.34	10.11	0.014
BMI (kg/m^2)	1,823	25.48	3.90	26.43	4.74	0.001	24.57	3.43	0.000
HbAlc (%)	1,713	8.09	1.81	8.35	1.81	0.020	9.28	2.92	0.002
SBP (mmHg)	1,825	130.82	16.65	134.53	17.73	0.000	140	23.67	<0.0001
DBP (mmHg)	1,825	76.57	10.67	77.02	11.57	0.505	77.81	11.57	0.696
Urine Cr (mg/dL)	1,827	118.0	80.8	104.6	68.6	Null[c]	16.2	21.1	Null
Urine Alb (mg/L)	1,827	17.7	14.6	56.9	33.9	Null	59.1	43.6	Null
Alb/Cr ratio	1,827	25.4	34.2	102.9	166.1	Null	520.5	398.8	Null
BUN (mg/dL)	301	16.56	7.85	19.49	8.62	0.009	17.72	3.59	0.033
Cr (mg/dL)	1,257	0.91	0.31	0.99	0.39	0.002	1.05	0.36	0.001
Albumin (g/dL)	84	4.09	0.70	4.10	0.68	0.975	4.30	0.26	0.880
TG (mg/dL)	1,362	143.64	99.94	140.94	84.01	0.650	199	118.9	0.049
HDL-c (mg/dL)	1,074	46.35	13.77	43.47	14.01	0.007	47.53	13.26	0.022
LDL-c (mg/dL)	900	115.44	34.01	122.00	34.81	0.018	130.44	35.16	0.019
UA (mg/dL)	512	5.83	1.79	6.01	1.71	0.348	5.71	1.90	0.624

AU = albuminuria; Alb = albumin; BMI = body mass index; BUN = blood urea nitrogen; Cr = serum creatinine; DBP = diastolic blood pressure; HDL-c = high-density-lipoprotein cholesterol; LDL-c = low-density-lipoprotein cholesterol; SBP = systolic blood pressure; SD = standard deviation; TG = triglycerides; UA = uric acid.

[a] The p value of t-test/Chi-squared test for normoalbuminuria and microalbuminuria comparison.

[b] The p value of analysis of variance/Chi-squared test for the comparison of three groups.

[c] Null means that no statistical testing was done, because urine Cr and urine Alb were the components of Alb/Cr ratio.

exercise, may explain an abnormal urine MAU test result.[8] Authors of the DEMAND Study admitted three limitations in their study, which were single random urine collection, nonpersistent MAU definition, and possible selection bias. These limitations were virtually avoided in our study, which may contribute to the relatively low MAU prevalence found.

The cumulative risk effect of age and DM duration described a very different pattern. For every 1-year increase in DM duration, there was a nearly constant risk of developing MAU, whereas for age, the risk effect rose sharply after 60 years of age. Using multivariate logistic regression, there was a 1.022-fold risk for every 1-year increase in DM duration (the estimated odds ratio was 1.022 with 95% CI of 1.004−1.040, after adjusting for center and gender effect). Therefore, a policy of yearly screening of MAU is recommended once the diagnosis of diabetes is made and even more often for patients older than 60 years (e.g. every 6 months).

Concerning the screening methodology (two out of three determinations for the MAU diagnosis standard), the conditional probability approach provided an estimate for the

Table 3
The multivariate logistic regression of micro- and macroalbuminuria

Variables	Model 1[a]				Model 2[a]			
	OR	95% CI		p	OR	95% CI		p
Age (> 60 *vs.* ≤60)	1.70	1.31	2.19	0.000	1.73	1.27	2.36	0.000
Gender (female *vs.* male)	0.93	0.72	1.20	0.554	1.06	0.76	1.46	0.747
Waist (abnormal *vs.* normal)[b]	1.52	1.17	1.97	0.002	1.54	1.13	2.10	0.006
HbA1c (per 1%)	1.12	1.05	1.20	0.001	1.10	1.02	1.19	0.017
SBP (> 130 *vs.* ≤130)	1.68	1.27	2.22	0.000	1.91	1.37	2.65	0.000
DBP (> 80 *vs.* ≤80)	0.85	0.63	1.15	0.295	0.95	0.66	1.35	0.775
Creatinine (abnormal *vs.* normal)[c]					1.97	1.19	3.07	0.007
Effective n	1,685				1,181			

CI = confidence interval; DBP = diastolic blood pressure; OR = odds ratio; SBP = systolic blood pressure.

[a] The two models have adjusted center effect.

[b] Abnormal waist circumference: > 80 cm for females and > 90 cm for males.

[c] Abnormal creatinine level: > 1.4 mg/dL for females and > 1.5 mg/dL for males.

relationship among these screenings. It can be interpreted that patients with the first MAU testing had 66.7% chance to get the second MAU diagnosis, and the same interpretation can be made for the other conditional probabilities in Table 1. Added up, the three concordant pairs of the first and second screening results had 69.2% agreement in this study. In the Shanghai study, this agreement was reported to be 73.3% for the first versus the second screening.[9] In clinical practice, the estimated probability in Table 1 can be used to identify the high-risk MAU patients with noncompliant screening, because around 7.0% of patients may have negative result at the first screening followed by two positive results for MAU in the subsequent two screenings. Thus, it is still worth completing all three screening tests within 6 months when the first screening shows normoalbuminuria. Because of the limitations of our study, further study is needed to figure out the risk parameters for FN patients in the first MAU screening test.

Recently, several articles reported the MAU prevalence in Asian countries. MAU was found in 41.4% of T2DM population in Shanghai, China, and in 13.7% of the Japanese general population.[10] Because of a different study design, it is difficult to compare their findings. Generally speaking, hospital-based, nonrandom selection and single-screening design tend to produce higher prevalence estimates. Our study seems to show reasonably lower prevalence compared with the Microalbuminuria Asian Prevalence and DEMAND Studies. Theoretically, our survey should be a better representative of the real MAU prevalence in Taiwan T2DM population. The Shanghai study, using a population-based, randomized cluster sampling and three screenings measured by radioimmunoassay (although without using conditional probability approach), gave a very high prevalence of MAU in the downtown citizens older than 30 years.[11] In our survey, the prevalence of MAU was 27.0% in T2DM patients aged 31−80 years. The Japanese study, which targeted an older (older than 40 years) general population in a nonrandom selection, single-screening fashion, showed a relatively lower prevalence of MAU of 13.7% (relatively half of the expected prevalence in T2DM patients). In our survey, the prevalence of MAU was 27.5% in T2DM patients aged 41−80 years.

Obviously, using a single positive urinary screening test will give a remarkably high FP rate for the diagnosis of MAU, whereas adopting two positive out of three urinary screenings reveals more conservative and accurate results. Our method in this study of using a commercialized dipstick assay and a simplified three-urine-screening process provide the convenience of clinical practice and cost-effectiveness with more reliable diagnosis of MAU. As far as prevention or intervention in public health is concerned, our method can avoid unnecessary cost and provide more reliable intervention outcome measurements by reducing the huge FP rate (from 65.7% to 5.6%).

The prevalence of CKD Stage 3−5 (CKD Stage ≧3) in Taiwan was reported as 6.9% from a national population-based study[12] and 7.13% from a national standard medical screening program.[13] In our hospital-based study, the prevalence of CKD Stage ≧3 was 13.7% in T2DM patients, almost twice that previously reported. A community-based study among T2DM patients in Kinmen, Taiwan, also reported the prevalence of CKD Stage ≧3 to be 15.1%.[14] There are limitations in our study, however. For example, the serum creatinine level was recorded within the latest 6 months from the first screening, not exactly on the same day of recording of the urine MAU level. For those with MAU or macroalbuminuria, T2DM patients would have a 23.3% chance to be at CKD Stage 3 or higher. Although the association between CKD stage level and MAU or macroalbuminuria was significant, the strength of the association needs to be confirmed by long-term follow-up.

Concerning the issue of antihypertensive treatment in MAU prevention, the GUARD Study reported that ACE inhibitor with diuretic contributed a lot of albuminuria normalization for T2DM patients with only MAU and hypertension.[15] A target blood pressure less than 130/80 mmHg in T2DM patients was recommended by ADA.[16] Furthermore, ACE inhibitor or ARB regimen was recommended as an antihypertensive therapy for T2DM patients with hypertension by AHA−ADA.[17] In this study, drug usage data were collected from the medical records within the latest 6 months before the first visit, while all MAU patients were new diagnosed within 6 months after the first visit. Therefore, we could observe what kind of drugs may have less frequency of MAU. Our results showed that ACE inhibitor treatment group had the lowest percentage of MAU, that is, 18.7%, but this finding did not reach statistically significant level. The most frequent of the two-drug combination therapy was ARB plus calcium channel blockers; ACE inhibitor plus diuretic was the fourth in frequency. Among patients without antihypertensive treatment, there were still 49.2% with blood pressure greater than the target level. The onset and detection of MAU represents the diagnosis of early stage of diabetic nephropathy and correlates with early stage of other diabetic complications, such as diabetic autonomic neuropathy.[18] Therefore, early awareness and aggressive glycemic and blood pressure control are warranted.[19−21]

In conclusion, this study demonstrates the application of conditional probability method to justify the rationale for adopting two positive out of three urinary screening tests for the diagnosis of MAU. An adjusted prevalence rate of MAU as 26.9% is reported. These results may provide a basis for cost−benefit consideration in designing preventive and interventional policies in public health. Furthermore, these results are associated with the need for strengthening and promoting of the awareness and practice of early detection and monitoring of renal and cardiovascular risk factors in DM patients.

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