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Relationship between prevalence and associated risk factors of microalbuminuria in middle-aged and elderly populations.

Hai Yu[1], Baohe Zhang[2], Ji Wang[2], Mingxu Li[1*]

[1]Department of Nephrology, Navy General Hospital, Beijing, PR China

[2]Department of Cadres Medical Care, Navy General Hospital, Beijing, PR China

Abstract

This study aimed to investigate and explore the prevalence and associated risk factors of Microalbuminuria (MAU) in middle-aged and elderly populations. A total of 1,086 middle-aged and elderly populations who underwent physical examination in our hospital were selected using the randomized cluster sampling method for the health questionnaire survey in April 2013. Related laboratory index tests were also performed to analyze the prevalence and associated risk factors of MAU that may possibly affect the urinary albumin/creatinine ratio. A total of 139 MAU patients were selected (detection rate, 12.80%), including 119 men and 20 women. Statistical significance was not observed between the two groups (P>0.05). The logistic regression analysis showed that age (Odds Ratio (OR)=1.038), fasting blood glucose (OR=1.533), and waist circumference (OR=1.033) were the independent risk factors of MAU in men. The prevalence of MAU in Chinese middle-aged and elderly populations is similar to those reported in other countries. The related risk factors should be closely monitored and addressed as early as possible to prevent the progress of kidney diseases.

Keywords: Microalbuminuria, Prevalence, Related factors.

Abbreviations:

MAU: Microalbuminuria; NAU: Normal Albuminuria; ACR: Albumin/Creatinine Ratio; CKDs: Chronic Kidney Diseases; SBP: Systolic Blood Pressure; BMI: Body Mass Index; TG: Triglyceride; TC: Total Cholesterol; HDL: High Density Lipoprotein Cholesterol; LDL: Low Density Lipoprotein Cholesterol; UA: Uric Acid; FPG: Fasting Plasma Glucose; 2hPG: 2-h Plasma Glucose; Hcy: Hyperhomocysteinemia.

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Introduction

Chronic Kidney Diseases (CKDs) are highly prevalent in many developing countries. Among which, Microalbuminuria (MAU) is not only an early manifestation but also a sign of systemic vascular endothelial injury [1-3]. Recent studies proved that MAU is an important risk factor for cardiovascular diseases, which can predict the occurrence and development of atherosclerosis-related ischemic cardiovascular events, and is closely related to the severity of coronary artery diseases [4-6]. Chinese and foreign epidemiological surveys have indicated significant correlations of MAU with the occurrence of coronary heart disease, hypertension, heart failure, diabetes, metabolic syndrome, or acute cerebrovascular disease [7-9]. Clinical data have also confirmed that patients with high-risk factors of cardiovascular diseases were significantly correlated with left ventricular hypertrophy, carotid intima thickening, and subclinical cardiovascular diseases and MAU [10-14]. MAU is also a predictor of all-cause mortality in the general populations [15]. Occurrence of MAU can be considered as a sign of CKDs and cardiovascular diseases and also help in identifying the beneficiaries of the preventive measures against cardiovascular diseases. In this study, the cluster sampling method was used to detect the prevalence of MAU in the middle-aged and elderly populations and preliminarily explored the factors that may affect MAU.

Materials and Methods

Participants

Some middle-aged and elderly populations from a government office who underwent physical examination in our hospital were enrolled using the cluster sampling method for the health questionnaire survey and laboratory-related index detection in April 2013. The exclusion criteria were positive results of urine protein during the urine routine test, fever, strenuous exercise, congestive heart failure, or haematuria. A total of 1,086 participants were included in this study (Table 1). This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics

Committee of Navy General Hospital. Written informed consent was obtained from all participants.

Table 1. Basic information of the study subjects.

Parameter	All subjects (n=1086)	Males (n=977)	Females (n=109)
Age (y)	58.96 ± 10.56	59.02 ± 10.58	58.40 ± 10.38
BMI (kg/m^2)	25.25 ± 2.78	25.41 ± 2.76	23.80 ± 2.59
Waist circumference (cm)	88.23 ± 8.38	89.20 ± 7.89	79.25 ± 7.48
SBP (mmHg)	131.60 ± 14.59	132.07 ± 14.38	127.36 ± 15.83
DBP (mmHg)	82.02 ± 10.30	82.66 ± 10.23	76.35 ± 9.09
SCr (μmol/L)	87.45 ± 12.69	89.35 ± 11.65	70.48 ± 8.22
TG (mmol/L)	1.63 ± 1.18	1.66 ± 1.22	1.32 ± 0.66
TC (mmol/L)	5.18 ± 0.96	5.14 ± 0.97	5.54 ± 0.76
HDL (mmol/L)	1.49 ± 0.33	1.46 ± 0.32	1.78 ± 0.32
LDL (mmol/L)	2.92 ± 0.65	2.91 ± 0.66	3.06 ± 0.59
UA (μmol/L)	322.60 ± 73.93	321.35 ± 70.53	244.17 ± 55.25
FPG (mmol/L)	5.93 ± 0.98	5.98 ± 1.01	5.48 ± 0.52
2hPG (mmol/L)	6.65 ± 2.25	6.75 ± 2.32	5.81 ± 1.16
HbA1c (%)	5.67 ± 0.51	5.68 ± 0.52	5.61 ± 0.35
Hcy (μmol/L)	12.98 ± 7.40	13.49 ± 7.54	8.35 ± 3.40

Survey contents

General characteristics, height, weight, waist circumference, hip circumference, blood pressure, Albumin/Creatinine Ratio (ACR), and various related biochemical indexes were included in the survey questionnaires.

Detection methods

One mercury sphygmomanometer was used to measure the blood pressure from the right upper arm and in sitting position, taken after quietly sitting for 15 min. Diagnostic criteria of hypertension are systolic blood pressure (SBP) of ≥ 140 mmHg and/or Diastolic Blood Pressure (DBP) of ≥ 90 mmHg in patients with history of hypertension and currently taking antihypertensive drugs.

The morning urine of each participant was tested for ACR using kinetic nephelometry (BECKMAN COULTER, America). The creatinine was tested using the basic picric acid method (COBAS INTEGRA 400 plus, Roche, Switzerland). ACR was then calculated, and participants with ACR of 30-300 mg/g were defined as MAU.

One Hitachi 7180 (Roche Diagnostics, Germany) was used to evaluate fasting and 2-h postprandial venous blood glucose from each participant in detecting related biochemical parameters. High-performance liquid chromatography was used to determine the glycosylated hemoglobin (HbA1c).

The height, weight, and waist and hip circumference were measured by uniformly trained physicians or nurses. Each parameter was measured twice per participant to obtain the average.

Statistical analysis

SPSS 16.0 statistical software was used for data processing and analysis; the measured data were expressed as ($\bar{x} \pm s$) using the t-test. The count data were compared using the χ^2 test. The correlative factors were analyzed using univariate and unconditional multivariate logistic regression analysis. The relative risk was estimated using Odds Ratio (OR) and 95% Confidence Interval (CI), with $P<0.05$ considered as statistical significance.

Results

Comparison of MAU incidence

A total of 139 MAU cases were selected out of the 1,086 study participants, with the detection rate of 12.80%. Among the 977 men, 119 had MAU, with the detection rate of 12.18%, whereas in 109 females, 20 had MAU, with the detection rate of 18.35%. Significant difference in the detection rate of MAU between men and women was not observed ($\chi^2=3.34$, $P>0.05$).

Univariate analysis of MAU

After stratifying based on genders, a total of 15 MAU-related variables were compared between the groups with Normal Albuminuria (NAU) or MAU. The measurement data were analyzed using the t-test, and the count data were analyzed using the χ^2 test to analyze the factors that may affect MAU.

In male participants, age, SBP, Total Cholesterol (TC), Low-Density Lipoprotein (LDL), Fasting Plasma Glucose (FPG), 2-h Postprandial Glucose (2hPG), HbA1c, and waist circumference show statistical significance between the two groups (Table 2).

Table 2. *Univariate analysis of MAU in male subjects (n=977).*

Parameter	NAU (n=858)	MAU (n=119)	P
Age (y)	58.34 ± 10.32	63.93 ± 11.14	<0.001
BMI (kg/m^2)	25.38 ± 2.71	25.63 ± 3.11	0.362
Waist circumference (cm)	88.91 ± 7.59	91.22 ± 8.53	0.002
SBP (mmHg)	131.41 ± 14.15	136.87 ± 15.14	<0.001
DBP (mmHg)	82.57 ± 9.92	83.24 ± 12.32	0.503
SCr (μmol/L)	89.15 ± 10.70	90.79 ± 16.96	0.306
TG (mmol/L)	1.66 ± 1.24	1.66 ±1.09	0.981
TC (mmol/L)	5.18 ± 0.98	4.87 ± 0.83	0.001
HDL (mmol/L)	1.46 ± 0.32	1.43 ± 0.31	0.393
LDL (mmol/L)	2.94 ± 0.66	2.70 ± 0.63	<0.001
UA (μmol/L)	331.50 ± 67.81	330.23 ± 88.01	0.879
FPG (mmol/L)	5.91 ± 0.90	6.46 ± 1.50	<0.001
2hPG (mmol/L)	6.60 ± 2.10	7.80 ± 3.32	<0.001
HbA1c (%)	5.66 ± 0.49	5.83 ±0.70	0.01
Hcy (μmol/L)	13.49 ± 7.73	13.54 ± 6.03	0.945

In female participants, SBP, TG, HDL, FPG, 2hPG, and waist circumference were statistically significant between the two groups (Table 3).

Table 3. *Univariate analysis of MAU in female subjects (n=109).*

Parameter	NAU (n=89)	MAU (n=20)	P
Age (y)	57.30 ± 9.26	63.30 ± 13.60	0.073
BMI (kg/m^2)	23.80 ± 2.43	23.75 ± 3.27	0.944
Waist circumference (cm)	78.58 ± 7.03	82.10 ± 7.59	0.049
SBP (mmHg)	124.64 ± 13.78	139.45 ± 18.91	<0.001
DBP (mmHg)	75.90 ± 9.11	78.35 ± 8.97	0.278
SCr (μmol/L)	70.67 ± 8.56	69.64 ± 6.58	0.614
TG (mmol/L)	1.26 ± 0.61	1.62 ± 0.78	0.027
TC (mmol/L)	5.58 ± 0.80	5.35 ± 0.57	0.204
HDL (mmol/L)	1.81 ± 0.31	1.64 ± 0.35	0.032
LDL (mmol/L)	3.09 ± 0.61	2.94 ± 0.43	0.283
UA (μmol/L)	239.93 ± 54.35	263.05 ± 56.66	0.091
Fasting blood sugar (mmol/L)	5.42 ± 0.50	5.78 ± 0.51	0.005
Postprandial 2-h blood sugar (mmol/L)	5.70 ± 1.15	6.33 ± 1.12	0.033
HbA1c (%)	5.59 ± 0.35	5.71 ± 0.33	0.165
Hcy (μmol/L)	8.49 ± 3.36	7.71 ± 3.58	0.356

Multivariate logistic regression analysis

As female participants were fewer, no multivariate logistic regression analysis was performed. In male participants, the existence of MAU was set as the dependent variable, with 1 considered as positive (ACR, 30-300 mg/g) and 0, as negative (ACR<30 mg/g). The age, waist circumference, SBP, TC, LDL, FPG, 2hPG, and HbA1c were included in the multivariate logistic regression analysis, and finally, the statistically significant risk factors were included (α=0.05, 0.10). The results show that age, FPG, and waist circumference are the risk factors of MAU in men (P<0.05, Table 4).

Table 4. *Multivariate logistic regression analysis of MAU-related variables in males.*

Variable	β	SE	Wald	P	OR (95% CI)
Age	0.037	0.011	12.015	0.001	1.038 (1.016~1.059)
SBP	0.012	0.007	2.763	0.096	1.012 (0.998~1.027)
LDL	-0.432	0.297	2.118	0.146	0.649 (0.363~1.161)
FPG	0.427	0.154	7.646	0.006	1.533 (1.132~2.074)
2hPG	0.019	0.059	0.1	0.752	1.019 (0.908~1.143)
HbA1c	-0.389	0.277	1.974	0.16	0.678 (0.394~1.166)
Waist circumference	0.033	0.013	6.34	0.012	1.033 (1.007~1.060)
TC	0.021	0.218	0.009	0.924	1.021 (0.666~1.564)

Discussion

The incidence of MAU in the middle-aged and elderly populations investigated in this study was 12.80% (12.18% in men and 18.35% in women), with no significant difference based on gender. Previous studies have once reported that the incidence rates of MAU in the general populations were 7% and 3.8% by Prevend and Intermap, respectively [16,17]. However, Tanaka reported that the incidence of MAU in general Japanese populations was 4.6%, which is lower than that of our study [18]. This difference may be because our study participants were older. Takahata reported an incidence rate of 13.7%, which is consistent with our results [19].

In this study, a total of 15 variables were possibly related to MAU, including demographic characteristics, physical examination indexes, and biochemical indexes. Significant

differences were observed in the SBP, triglyceride, HDL, fasting blood glucose, 2hPG, and waist circumference between the female NAU and MAU groups. Due to a fewer number of female MAU patients, no multivariate logistic regression analysis was performed. However, in male populations, significant differences were observed in age, SBP, total cholesterol, LDL, fasting blood glucose, 2hPG, HbA1c, and waist circumference between the NAU and MAU groups. Further multivariate logistic regression analysis showed that age, FPG, and waist circumference were the risk factors of MAU in men ($P<0.05$). These results are not completely consistent with those of the previous studies.

Previous studies concluded that MAU is significantly associated with metabolic syndrome, and certain studies considered that body mass index, hypertension, diabetes, triglycerides, high-sensitivity C-reactive protein, and alcohol intake were major risk factors of MAU [20-22]. Our study showed that only fasting blood glucose and waist circumference were the risk factors of MAU, which is partially consistent with those of the other studies. Although diabetes was included in the study, data were collected from a physical examination, which was also from the real world. Whether, with or without diabetes, FPG was one of the risk factors. In this study, a statistical significance was observed in the SBP between the NAU and MAU groups. However, the multivariate regression analysis did not show the same result, which may be related to the fact that clinicians and patients focused more on hypertension that can be effectively treated using oral antihypertensive drugs.

The relationship between MAU and hypertension, hyperglycemia, and obesity has been demonstrated in various populations [23,24]. Regarding the mechanisms, a large number of studies have shown that the mutual actions among hypertension, dyslipidaemia, and insulin resistance are mediated by the activation of redox-sensitive pathways, renin-angiotensin system, or lectin-like oxidized low-density lipoprotein 1 (LOX-1) [25]. In addition, among the inflammatory reactions mediated by the reactive oxygen species, these redox-sensitive transcription factors as nuclear factor-κB (NF-κB) also play important roles [26]. In diabetic patients, the degree of urinary protein is related to NF-κB upregulation [27]. The activation of NF-κB can promote the expressions of proinflammatory cytokines, such as tumor necrosis factor (TNF)-α and interleukin-6, and then further stimulate the production of C-reactive protein. This may also explain the association between the C-reactive protein and metabolic syndrome. In rat glomerulonephritis model, blocking TNF-α can relieve proteinuria [28]. Therefore, endothelial cell injury, oxidative stress, and inflammatory responses are important factors linking MAU with the metabolic syndrome and coronary heart diseases [29,30]. Hirose also suggested that the urinary excretion of 5-hydroxytryptamine and the ratio of 5-hydroxytryptamine to dopamine in MAU patients are significantly higher than non-MAU populations [31].

MAU is an important indicator reflecting systemic vascular endothelial cell injuries, and current studies have further extended the occurrence of MAU from patients with cardio cerebrovascular diseases, atherosclerosis, and diabetes to the general populations [18,32]. Prevend observed that MAU and all-cause mortality are linearly associated [16]. In HOPE's study, the adjusted risk of major cardiovascular events will be increased by 5.9% for each 0.4 mg/mmol increase of urinary ACR [15]. These studies have confirmed that even a small increase of the urinary albumin excretion rate within the normal range will increase the risk of cardiovascular events. Reduced urinary albumin is also associated with decreased cardiovascular events. Other studies also suggested that in the so-called healthy populations (without history of cardiovascular diseases, hypertension, or diabetes), the presence of cardiovascular diseases, hypertension, and diabetes in isolated MAU patients is significantly higher than those without MAU as revealed in the subsequent follow-up [33].

Therefore, with the improvement of Chinese economic level and people's standard of living, the prevalence of MAU has increased. As MAU has a better predictive value toward cardiovascular diseases, kidney diseases, and overall survival in the general populations and is clinically easy to implement, MAU screening should be conducted in middle-aged and elderly populations as well as those with metabolic abnormalities [34].

Conflicts of Interest

The authors declare no conflict of interest.

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*Correspondence to

Mingxu Li

Department of Nephrology

Navy General Hospital

Beijing

PR China