Prevalence and associated factors of microalbuminuria in Chinese individuals without diabetes: cross-sectional study

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ABSTRACT

Objective: To investigate the prevalence of microalbuminuria (MAU) among Chinese individuals without diabetes and the relationship between MAU and metabolic factors, individual socioeconomic status (SES), and regional economic development level.

Design: Cross-sectional study of prevalence of MAU.

Setting: 152 urban street districts and 112 rural villages from northeast, north, east, south central, northwest and southwest China.

Participants: 46 239 participants were recruited using a multistage stratified sampling design from 2007 to 2008. A total of 41 290 participants without diabetes determined by oral glucose tolerance test were included in the present study. Urine albumin/creatinine ratio results of 35 430 individuals were available.

Primary and secondary outcome measures: Positive detection of MAU was determined using an ACR of 22.1–299.9 mg/g in men 30.9–299.9 mg/g in women.

Results: The prevalence of MAU in men was 22.4% and 24.5% in women. In developed, intermediate-developed and under-developed areas, the prevalence of MAU in men was 20.7%, 21.9% and 32.5%, respectively; in women the prevalence was 19.6%, 26.0% and 29.5%, respectively. The prevalence of MAU increased as the number of metabolic disorders present increased, and as the number of lower SES components increased (farmer, below university education level and low income). Prevalence of MAU in developed and intermediate developed areas had adjusted risk ratios of 0.52 (95% CI 0.42 to 0.60) and 0.65 (95% CI 0.57 to 0.76), respectively. Multivariate logistic analyses demonstrated MAU was strongly associated with older age, high-blood pressure, higher blood glucose low education level, low occupational level and residence in under-developed region.

Conclusions: Several factors had independent correlations to MAU in China: older age, metabolic abnormalities, lower SES level and living in economically under-developed areas, which encourage the development of strategies to lower the risk for MAU in these susceptible populations.

INTRODUCTION

Microalbuminuria (MAU) is defined as a urinary albumin excretion ranging from 30 to 299 mg/24 h, and is a marker for chronic kidney damage and a risk factor for the progression of chronic kidney diseases (CKDs), cardiovascular disease (CVD) and cerebrovascular disease and mortality.1–3 The prevalence of MAU has been shown to vary within and between populations. For example, an analysis of data from the Third National Health and Nutrition Examination Survey, found the prevalence of MAU in the general US population was 6.1% for men and 9.7% for women.4 The prevalence of MAU has been estimated at 6% in Australians,5 6.6% in Netherland,3 20% in native Canadians6 and 36.9% in Singaporeans ≥40 years.7 Prevalence estimates from the same areas of

Strengths and limitations of the study

- This is the first study on prevalence of microalbuminuria in Chinese individuals, that is based on a large population-based sample from diverse economic levels, with analyses accounting for the complex sampling design in order to provide a representative sample of 14 Chinese provinces.
- The use of radioimmunoassay methods in urine albumin measurement increased sensitivity.
- A limitation of this study is that it is cross-sectional and could not demonstrate cause–effect relationship.
Shanghai, China have varied widely between 5% and 19.4%. Factors that may have caused dissimilar prevalence estimates include varying definitions of MAU and different study methodologies. The excretion rate of urine albumin is unstable and may be affected by physiological factors such as sports participation and body position. High-performance liquid chromatography to determine urinary albumin concentrations revealed higher values compared to nephelometry, especially in the lower concentration range, which resulted in a higher prevalence of MAU. The urinary microalbuminuria/creatinine ratio method has been recommended due to a lack of reliable 24 h urine collection methods.

Risk factors for MAU and kidney diseases include components of the metabolic syndrome (MS) and lower SES. Higher odds for MAU have been found in Singaporeans with lower educational attainment (OR=1.76, 95% CI 1.23 to 2.52), lower income in retirement (OR=1.64, 95% CI 1.16 to 2.31), smaller housing type (OR=1.44, 95% CI 1.01 to 2.06) and coexistence of multiple low-SES factors (OR=2.37, 95% CI 1.56 to 3.60). Whereas affluence has been shown to be protective against CKD among blacks in the USA, higher occupational grade has been shown to be protective among whites in Europe.

There are many international epidemiological studies on MAU, especially in diabetic populations, but there are few studies in non-diabetic Chinese populations. As the Chinese economy has developed over the last 30 years, the prevalence of metabolic diseases has increased with varying estimates in different parts of China. We reported that the prevalence of diabetes was not only associated with personal metabolic factors, but also with personal socioeconomic factors and regional economic development levels. The aim of the present study was to explore prevalence of MAU in China people without diabetes and to examine the relationship between MAU and metabolic factors (such as obesity, hypertension, hyperglycaemia and hypertriglyceridaemia), individual SESs (education, income and occupation) and regional economic development levels.

METHODS
Subjects and experimental design
A multistage stratified sampling design was used to select participants that were greater than 20 years in age throughout 14 Chinese provinces. A detailed description of the study population and methodology has been published previously. A total of 46,299 participants were recruited that included 41,290 participants without diabetes as determined by an inquiry of disease history and physical examination. Impaired fasting glucose (IFG) was defined as a fasting glucose level greater than or equal to 1.7 mmol/L, or HDL-c at a level less than 0.9 mmol/L for men and 1.0 mmol/L for women. Impaired fasting glucose (IFG) was defined as a fasting glucose level greater than or equal to 1.7 mmol/L, or HDL-c at a level less than 0.9 mmol/L for men and 1.0 mmol/L for women. Impaired fasting glucose (IFG) was defined as a fasting glucose level greater than or equal to 1.7 mmol/L, or HDL-c at a level less than 0.9 mmol/L for men and 1.0 mmol/L for women. Impaired fasting glucose (IFG) was defined as a fasting glucose level greater than or equal to 1.7 mmol/L, or HDL-c at a level less than 0.9 mmol/L for men and 1.0 mmol/L for women.

Prior to conducting the assessments, interviewers received training on the questionnaire and how to explain each item to increase the reliability. Waist circumference, weight and height were measured using standard methods. Blood pressure (BP) was measured two separate times at 5 min apart while participants were in the sitting position using an upright standard sphygmomanometer. The study followed the tenets of the Declaration of Helsinki. Informed consent from the participants was obtained after explaining the nature and possible consequences of the study procedures.

Blood was drawn from the antecubital vein in the morning after fasting for 10–14 h following 3 days of normal activity and diet. Blood samples were tested for total cholesterol, high-density lipoprotein cholesterol (HDL-c), triglycerides and plasma glucose (PG) levels. OGTTs 75 g were then performed 0.5 h later followed by another blood draw 2 h later. In addition, spot urine specimens were collected in the morning to measure ACR. All assessments were performed using a standard protocol that conformed to the international standards for definitions and measurements. PG was determined using the hexokinase method. Urine albumin concentration and serum level of immune reactivity insulin were measured using radioimmunoassay (RIA) in the central laboratory (North Biotechnology Institute, Beijing, China; inter- and intra-assay coefficients of variation <5%). The picric acid method was used to measure the level of urine creatinine in the central laboratory. ACR was calculated as the urine microprotein (mg/L) divided by urinary creatinine (g/L), with urine creatinine levels less than 0.5 mg/g defined as missing values.

MAU and covariates
Patients with diabetes, as diagnosed according to the 1999 WHO criteria were excluded from the analyses. MAU was defined as a urinary ACR in the range of 21.1–299.9 mg/g in men and 19.9–299.9 mg/g in women. Central obesity was defined as a waist circumference greater than 90 cm in men and greater than 80 cm in women. Overweight was defined as a body mass index (BMI) greater than 25 kg/m² and less than 30 kg/m² and obesity was defined as a BMI greater than 30 kg/m². Hypertension was defined as the participant having a history of high BP or BP greater than 140/90 mm Hg. Dyslipidaemia was defined as triglyceride at a level greater than or equal to 1.7 mmol/L, or HDL-c at a level less than 0.9 mmol/L for men and 1.0 mmol/L for women. Impaired fasting glucose (IFG) was defined as a fasting glucose level greater than or equal to 1.7 mmol/L, or HDL-c at a level less than 0.9 mmol/L for men and 1.0 mmol/L for women.

Figure 1  Prevalence of microalbuminuria (MAU) in various categories in Chinese without diabetes. (A) Age and sex-specific prevalence of MAU. (B) Prevalence of MAU in different obesity, blood pressure and insulin sensitivity index groups. (C) Prevalence of MAU in different education level, income level, profession and socioeconomic status level groups. *p Trend <0.001 among age groups, †p<0.001 men vs women in corresponding age subgroups; ‡p<0.01 in different ISI, BMI, blood pressure, glucose tolerance, economic developed areas, education level, incomes and profession groups; #p<0.01 men vs women in corresponding subgroups. BMI, body mass index; HT, hypertension; IS, insulin sensitivity; IR, insulin resistance; IGR, impaired glucose regulation; NGT, normal glucose tolerance; NT, normal blood pressure.
as a fasting blood glucose level between 6.1 and 7.0 mmol/L, and 2-h post-load PG level less than 7.8 mmol/L. Impaired glucose tolerance (IGT) was defined as 2-h post-load PG level between 7.8 and 11.1 mmol/L, and a fasting PG level <6.1 mmol/L. Impaired glucose regulation (IGR) was defined as the presence of IFG or IGT. Matsuda insulin sensitivity index was calculated by the formula:

\[
\text{Matsuda ISI} = \frac{10,000}{\sqrt{(\text{Ins}_0 \times \text{FPG} \times 18 \times (\text{Ins}_0 + \text{Ins}_{30} + \text{Ins}_{120})/3 \times (\text{FPG} + \text{Glu}_{30} + \text{PG}_{2\text{h}})/18/3)}
\]

The value for the 25th percent in normal glucose tolerance (NGT) was determined as the cut-off value. Individuals with NGT values below the cut-off were defined as insulin resistant while all others were considered insulin sensitive.

**Statistical analyses**

SUDAAN software V.1.0 (Research Triangle Institute) was used to conduct weighted analyses to account for the complex stratified study design to adjust according to Chinese population data in 2006. Student's t tests were used to examine the differences between continuous variables and \(\chi^2\) tests for categorical variables. Logistic regression analyses were used to examine the prevalence of MAU by sex, age, education level, occupational level, incomes, metabolic status and economic level. All p values were two-sided using <0.05 as the level for significance.

**RESULTS**

Among the 41,290 participants (mean age 43.9 years, range 20–100 years) included in this study, 35,470 participants had ACR data. There were 125 (0.35%, comprised of males 0.31% and females 0.39%) individuals with macroalbuminuria, defined as ACR ≥ 300 mg/g. Among the qualified participants with MAU (300 > ACR ≥ 22.1 mg/g in men and 300 > ACR ≥ 30.9 mg/g in women), there were 24.4% in men (95% CI 23.6 to 25.4%) and 24.5% in women (95% CI 23.2 to 25.9%). The prevalence of MAU was higher in progressively increasing age categories both in men and in women (figure 1A).

MAU was more prevalent in individuals who were insulin resistant, hypertensive, had IGR and had higher BMI (figure 1B). MAU prevalence also varied by SES; residence in under-developed areas, lower educational attainment, lower income and occupation as a farmer were associated with an elevated prevalence of MAU (figure 1C).

Metabolic abnormalities that were examined included IGR, hypertension, high TG, a low level of HDL-c, central obesity and insulin resistance (IR). The participants were placed into six groups according to the number of metabolic problems. As expected, the number of metabolic problems was associated with an increased risk of MAU.
abnormalities increased the prevalence of MAU (figure 2A). Individuals from developed areas had significantly lower prevalence of MAU compared to intermediate-developed and under-developed groups that had a similar number of metabolic problems.

The SES components that were examined included occupation as a farmer, education level under university and annual family income less than CNY 30 000. The participants were placed into four groups according to the number of low-SES components present, and by the degree of development in the area in which they live (figure 2B). Prevalence of MAU increased as the number of low-SES components increased within different categories of development. There was higher prevalence of MAU in men who had 1 or less low-SES components. In those with 2–3 low-SES components, there was no significant difference between men and women in prevalence of MAU (figure 2C).

Sample characteristics according to ACR value quartiles are shown in table 1. Males had higher average metabolic values within each ACR quartile than females. Higher values for ACR were associated with higher prevalence of hypertension and higher values for other metabolic parameters.

The average MAU for males and females in intermediate-developed and developed areas were significantly lower than in under-developed areas (table 2). There were no age differences between the three
economic development areas; BMI, BP, blood glucose, insulin and IR were all higher in developed areas than in under-developed areas.

Three multivariate logistic models were used to examine the relationship between demographic data, metabolic factors, personal SES, rural/urban residence and regional economic development (table 3). In model 1, old age, increase of plasma glucose (PG) and hypertension were independently associated with MAU. In model 2, where SES components were included, low-education level and low annual family income category were also associated with MAU. In the model 3, individual residence, where regional economic development levels were added. The following variables were independently associated with MAU: older age, higher blood glucose, high BP, low-education levels, and low-regional economic development level.

**DISCUSSION**

**Statement of principal findings**

To our knowledge, this is the largest population-based study of MAU in Chinese individuals without diabetes. The prevalence of MAU was 24.4% in males and 24.5% in females. Individuals with higher level of ACR had higher prevalence of hypertension, obese/overweight and IGR (table 1). In contrast to the higher level of BP, PG, serum triglycerides and IR in economically developed regions, the level of ACR was lower in economically developed regions (table 2). Results from the multivariate analyses suggest that increasing age, high-BP and increased blood glucose were independent risk factors for MAU. Results from the univariate analyses suggested that MAU was more prevalent in participants with IR than those who were insulin sensitive. However, after adjusting for blood glucose level in multivariate analyses, IR was not significantly associated with MAU. The prevalence of MAU increased as the number of metabolic abnormalities increased in developed areas and in under-developed areas; over 50% of participants with five metabolic abnormalities in under-developed and intermediate-developed areas had MAU. Some low-SES parameters were associated with MAU. For example, the prevalence of MAU was higher in individuals with under a university education and in those who had low-annual family income. Level of regional economic development was significantly associated with MAU with the intermediate-developed and developed areas having 35% and 48% lower prevalence than under-developed areas, respectively. This association appeared to be independent of metabolic abnormalities and low SES.

**Strengths and limitations of the study**

Strengths of this study included the large population-based sample from diverse economic levels, with analyses accounting for the complex sampling design to provide a representative sample of 14 Chinese provinces; the use of RIA methods to test for urine albumin to increase sensitivity. The limitations of our study included the cross-sectional design that limited the ability to make cause-effect inferences, and the one-time collection of spot urine specimens due to a large variability in albumin excretion rates that did not allow an evaluation for the persistence of MAU.

**Comparison with other studies**

Both men and women in our study had a significantly higher prevalence of MAU compared to individuals in developed countries. Prevalence of MAU in the general US population was 6.1% in men and 9.7% in...
### Table 1 Characteristics of participants presented by ACR quartiles in Chinese men and women

<table>
<thead>
<tr>
<th>ACR (mg/g)</th>
<th>Men (Q1: 0.5–6.8)</th>
<th>Q2 (6.9–12.5)</th>
<th>Q3 (12.6–26.3)</th>
<th>Q4 (≥26.4)</th>
<th>Women (Q1: 0.5–6.8)</th>
<th>Q2 (6.9–12.5)</th>
<th>Q3 (12.6–26.3)</th>
<th>Q4 (≥26.4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=35 470</td>
<td>4265</td>
<td>3682</td>
<td>2960</td>
<td>2820</td>
<td>4589</td>
<td>5264</td>
<td>5839</td>
<td>6051</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41.1 (40.4–41.9)</td>
<td>42.8 (41.9–43.7)*</td>
<td>45.2 (44.2–46.2)*</td>
<td>48.3 (47.3–49.3)*</td>
<td>41.6 (40.8–42.4)</td>
<td>41.2 (40.5–42.0)</td>
<td>43.2 (42.4–44.0)*</td>
<td>47.6 (46.4–48.9)*</td>
</tr>
<tr>
<td>Overweight</td>
<td>26.8 (23.2–23.5)</td>
<td>27.9 (23.4–23.8)</td>
<td>29.0 (24.3–24.6)*</td>
<td>33.1 (30.2–36.1)*</td>
<td>19.9 (17.7–22.4)*</td>
<td>23.6 (21.6–25.7)*</td>
<td>21.7 (20.0–23.5)*</td>
<td>27.3 (25.1–29.7)*</td>
</tr>
<tr>
<td>Obese</td>
<td>4.3 (3.1–6.0)</td>
<td>5.5 (4.4–6.8)*</td>
<td>4.6 (3.5–6.7)</td>
<td>8.9 (7.3–10.9)*</td>
<td>4.2 (3.3–5.3)</td>
<td>3.3 (2.7–4.1)*</td>
<td>3.9 (3.2–4.8)</td>
<td>6.3 (5.2–7.5)*</td>
</tr>
<tr>
<td>Central obesity</td>
<td>24.2 (22.0–26.6)</td>
<td>24.8 (22.7–27.1)</td>
<td>24.7 (23.2–27.3)</td>
<td>31.9 (29.1–34.9)*</td>
<td>34.6 (32.0–37.4)*</td>
<td>34.8 (32.6–37.1)*</td>
<td>36.7 (34.5–38.9)*</td>
<td>45.9 (42.8–48.9)*</td>
</tr>
<tr>
<td>HTG</td>
<td>31.3 (31.0–33.8)</td>
<td>29.7 (28.8–34.0)</td>
<td>32.1 (29.3–35.0)</td>
<td>38.0 (35.0–41.1)*</td>
<td>21.1 (18.9–23.4)*</td>
<td>18.9 (17.1–20.8)</td>
<td>20.6 (18.9–22.5)*</td>
<td>27.0 (24.0–29.8)*</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15.8 (14.2–17.6)</td>
<td>24.0 (21.8–26.3)*</td>
<td>29.9 (27.2–32.7)*</td>
<td>43.0 (39.9–46.3)*</td>
<td>13.3 (11.4–15.5)</td>
<td>12.5 (11.2–13.9)*</td>
<td>19.5 (17.8–21.4)*</td>
<td>36.1 (33.0–39.4)*</td>
</tr>
<tr>
<td>IGR</td>
<td>15.8 (13.7–18.1)</td>
<td>17.2 (15.2–19.4)</td>
<td>18.7 (16.4–21.2)*</td>
<td>25.0 (22.3–27.8)*</td>
<td>13.4 (11.7–15.2)</td>
<td>13.8 (13.9–16.9)</td>
<td>15.4 (13.9–16.9)*</td>
<td>23.3 (20.4–26.4)*</td>
</tr>
<tr>
<td>IR</td>
<td>24.0 (21.8–26.4)</td>
<td>24.7 (22.4–27.2)</td>
<td>22.8 (20.4–25.4)</td>
<td>30.1 (27.3–33.1)*</td>
<td>22.5 (20.4–24.8)</td>
<td>23.4 (21.5–25.5)</td>
<td>24.0 (22.0–26.1)</td>
<td>28.0 (25.6–30.5)*</td>
</tr>
</tbody>
</table>

*p<0.05 vs ACR 0.5 to 6.8 mg/g.  
†p<0.05 vs men at same ACR quartiles.

ACR, albumin/creatinine ratio; HTG, serum triglyceride ≥1.7 mmol/L; IGR, impaired glucose regulation, IR, insulin resistant.
<table>
<thead>
<tr>
<th>Table 2</th>
<th>Clinical characteristics for men and women presented by level of economic development</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td><strong>Women</strong></td>
</tr>
<tr>
<td><strong>Age (year)</strong></td>
<td>43.7 (43.4, 44.0)</td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td>23.3 (23.2, 23.5)</td>
</tr>
<tr>
<td><strong>Waist circumference (cm)</strong></td>
<td>82.1 (81.6, 82.6)</td>
</tr>
<tr>
<td><strong>Systolic BP (mm Hg)</strong></td>
<td>119.1 (118.2, 120.0)</td>
</tr>
<tr>
<td><strong>Fasting PG (mmol/L)</strong></td>
<td>4.9 (4.9, 5.0)</td>
</tr>
<tr>
<td><strong>PG at 30' (mmol/L)</strong></td>
<td>8.1 (8.0, 8.2)</td>
</tr>
<tr>
<td><strong>PG at 120' (mmol/L)</strong></td>
<td>5.8 (5.7, 5.8)</td>
</tr>
<tr>
<td><strong>ACR (mg/g)</strong></td>
<td>14.1 (7.2, 27.1)</td>
</tr>
<tr>
<td><strong>Fasting serum IRI (mU/L)</strong></td>
<td>6.4 (4.8, 8.7)</td>
</tr>
<tr>
<td><strong>Serum IRI at 30' (mU/L)</strong></td>
<td>28.0 (16.6, 47.4)</td>
</tr>
<tr>
<td><strong>Serum IRI at 120' (mU/L)</strong></td>
<td>21.1 (11.8, 35.1)</td>
</tr>
<tr>
<td><strong>Total cholesterol (mmol/L)</strong></td>
<td>4.57 (4.52, 4.62)</td>
</tr>
<tr>
<td><strong>Triglycerides (mmol/L)</strong></td>
<td>1.23 (0.91, 1.89)</td>
</tr>
<tr>
<td><strong>HDL-c (mmol/L)</strong></td>
<td>1.25 (1.24, 1.27)</td>
</tr>
<tr>
<td><strong>HOMA-IR</strong></td>
<td>1.36 (1.00, 2.18)</td>
</tr>
<tr>
<td><strong>Matsuda ISI</strong></td>
<td>9.3 (6.5, 12.3)</td>
</tr>
</tbody>
</table>

*Significant difference compared with developed area, p<0.01.
†Significant difference compared with intermediate-developed area, p<0.01.

SI conversion factors: to convert insulin to pmol/L, multiple values by 6.945.

ACR, albumin creatinine ratio; BP, blood pressure; HDL-c, high-density lipoprotein-cholesterol;; IRI, immunoreactive insulin; ISI, insulin sensitivity index; PG, plasma glucose.
CONCLUSIONS

In conclusion, MAU was strongly associated with older age, metabolic abnormalities, lower SES and residence in lower economic development areas. It is suggested that future research studies explore the extent to which MAU could mediate the association between low-SES and metabolic, CVD and cerebrovascular disease.

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Competing interests None.

Patient consent Obtained.

Ethics approval The research ethics board of China-Japan Friendship Hospital approved this study.

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Data sharing statement No additional data are available.

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