BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031443
Article Type:	Research
Date Submitted by the Author:	04-May-2019
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Keywords:	Metabolic Syndrome, Microalbuminuria, Urinary Albumin

Association of Microalbuminuria and High-normal 24-hour Urinary Albumin Excretion with Metabolic Syndrome in the General Chinese Population

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Abstract

Objective: Microalbuminuria has been described as a risk factor for metabolic syndrome (MetS). However, the association between MetS components with microalbuminuria and 24-h urinary albumin excretion (UAE) has not been clearly explained in the general Chinese population. We aimed to analyze the association between microalbuminuria and high-normal 24-h UAE with MetS and its components.

Design: Cross-sectional observational study.

Setting: Four selected counties/districts in China's Shandong and Jiangsu Provinces.

Participants: A total of 2261 participants aged 18-69 years were included in this study. Participants with missing data on physical examination or incomplete urine collection are not included in the analysis.

Results: The prevalence of microalbuminuria was 9.0%, and the mean 24-h UAE was 18.0 mg/d. The prevalence of microalbuminuria was significantly higher for the MetS, high blood pressure, high triglycerides, low high-density lipoprotein cholesterol (HDL-C) and hyperglycemia groups, but not for central obesity. Both microalbuminuria and mean 24-h UAE were significantly increased with a number of MetS components. The adjusted odds ratio (OR) and 95% confidence interval (CI) for MetS with microalbuminuria was 2.95 (2.15-4.04) compared to those without microalbuminuria. Microalbuminuria patients were significantly associated with three components of MetS: high blood pressure, high triglycerides and hyperglycemia with OR=1.86, 95% CI 1.31-2.64; OR=1.80, 95% CI 1.31-2.46; and OR=1.84, 95% CI 1.34-2.53, respectively. No significant association of microalbuminuria and central obesity, low HDL-C was found. The presence of MetS were gradually elevated according to the normal range 24-h UAE quartiles: OR=1.00, OR=1.22, OR=1.14 and OR=2.02, respectively. Hyperglycemia was also significantly increased according to the normal range 24-h UAE quartiles.

Conclusions: Microalbuminuria and elevated 24-h UAE within normal range were closely associated with MetS in the Chinese population, which may provide a basis for the development of early

intervention to decrease the effects of MetS.

Keywords: Metabolic Syndrome; Microalbuminuria; Urinary Albumin

Strengths and limitations of this study

- We used 24-h UAE to define microalbuminuria, which was more accurate than most previous studies.
- This is the largest sample size of the general Chinese population collected 24-h urine.
- We explore the association between high-normal 24-h UAE with MetS and its components.
- This causal relationship between microalbuminuria and MetS cannot be demonstrated in our cross-sectional study.

INTRODUCTION

Microalbuminuria (MAU), defined by abnormally high albumin excretion (30-300 mg/d) in a 24-h urine sample, was significantly associated with chronic kidney disease, cardiovascular disease and progression of end-stage renal disease independent of traditional risk factors [1–4]. Prospective and epidemiologic studies have found that MAU is also a powerful predictor of all-cause and cardiovascular mortality in the general population [5-6].

Metabolic syndrome (MetS) is a widely accepted description of a cluster of metabolic abnormalities characterized by obesity, hypertension, dyslipidemia and hyperglycemia [7]. Some studies have evaluated the relationship between MetS and MAU as a marker for early-stage chronic kidney disease [8-11]. Significant associations between MetS and MAU have been demonstrated in the Japanese, [9] Korean [10, 12], and Chinese populations [13-16]. However, data concerning the relationship between individual MetS components and MAU were inconsistent, and a causal relationship between MAU and

MetS remains unclear despite the predictive value MAU has shown in the aforementioned studies. Furthermore, the study of the association between normal range 24-h urinary albumin excretion (UAE) and MetS components has been limited [15].

The amount of 24-h UAE is considered the 'gold standard' for defining MAU [17,18]. However, most of the previous studies of MAU in the Chinese population commonly used an early morning or random spot urine sample instead of measuring 24-h UAE. Therefore, in this study, we investigated the prevalence of MAU by analyzing 24-h UAE and analyzed the association between MAU and normal range 24-h UAE with MetS and its components.

METHODS

Study participants

Data were derived from the supplemental baseline survey of the Shandong Ministry of Health Action on Salt Reduction and Hypertension project, which was a cross-sectional survey conducted at four sites in the Shandong and Jiangsu provinces during 2013 and 2014. A total of 9600 participants aged 18-69 years were selected by a stratified, multistage sampling method. Demographic characteristics and lifestyle information were collected during a standardized interview. Each participant underwent a physical examination. A subsample of 2408 participants collected a single 24-h urine sample. Participants with the following conditions were not required to provide urine samples: (1) patients who had difficulty collecting a urine sample; (2) patients with acute and chronic urinary infection; (3) women who were pregnant, breastfeeding, or actively menstruating; and (4) patients with severe vomiting and diarrhea. We excluded 3 subjects with missing data from their physical examination or blood samples and 127 participants with incomplete 24-h urine collection. For the purpose of the present study on microalbuminuria, we also excluded 17 subjects with macroalbuminuria, or a 24-h UAE >300 mg/d.

Therefore, a total of 2261 participants were included in this study.

Our study was approved by the ethics committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention (201311). Written informed consent was obtained from all participants.

Demographic, anthropometrical and biochemical data collection

A face-to-face interview was conducted by local trained health professionals using a standard questionnaire. Relevant variables included age, sex, educational level, smoking status, alcohol intake, regular exercise and previous diagnosis and treatment of hypertension and diabetes. During physical examination, height, weight, waist circumference (WC) and blood pressure (BP) were measured by trained researchers using standardized protocols and techniques. Weight and height were measured with participants dressed in light, indoor clothing without shoes by standardized techniques and calibrated equipment. The waist circumference was measured at the narrowest point between the lower border of the rib cage and the iliac crest. The body mass index (BMI) was calculated as the weight in kilograms divided by the height in meters squared (kg/m^2). Blood pressure was measured three times by electronic sphygmomanometer (HEM-7071, Omron Corporation, Japan), and the final blood pressure was obtained by averaging the three measurements.

Fasting blood samples collected from each participant were processed and shipped in cold storage to a certified laboratory (ADICON Clinical Laboratory Inc., Jinan, China). Fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured. Plasma glucose was measured using a modified hexokinase enzymatic method. Serum cholesterol and triglyceride levels were analyzed enzymatically using commercially available reagents.

24-h Urine collection and analysis

Eligible participants were instructed not to change their dietary and lifestyle habits. We provided a standard plastic container for each participant to collect a 24-h urine sample. Trained researchers gave each participant both written and verbal instructions on how to collect a 24-h urine sample. Health professionals carefully explained to the subjects the purpose of the 24-h urine collection and asked the subjects to correctly repeat the information. The exact 24-h urine collection time, including starting and ending times, was recorded by the supervising health professional. The total volume of the collection was measured by a laboratory technician, and urine aliquots were frozen at −20°C and shipped to ADICON Clinical Laboratory in Jinan. Urinary creatinine was measured by the picric acid method. UAE was measured with an immunonephelometric method using the Olympus AU640 Analyzer, for which the coefficient of variation was 3.0%. Either a 24-h urinary volume less than 500 ml or a 24-h urinary creatinine volume that was ±2 standard deviations (SD) outside of the sex-specific mean, 0.98 to 16.17 mmol/l for men and 0.93 to 13.60 mmol/l for women, was defined as an incomplete urine collection [19].

Definition of the metabolic syndrome

We adopted the harmonized criteria of MetS, which defines MetS as the presence of ≥3 of the following risk factors [20]: central obesity defined as a WC ≥90 cm in men and ≥80 cm in women; high BP defined as a systolic blood pressure (SBP) ≥130 mmHg, a diastolic blood pressure (DBP) ≥85 mmHg or undergoing treatment with an antihypertensive medication; high triglycerides defined as a fasting plasma TC level ≥1.7 mmol/l or drug treatment for increased TC; low HDL-C defined as HDL-C <1.0 mmol/l in men and <1.3 mmol/l in women or drug treatment for increased HDL-C; or hyperglycemia defined as FBG level ≥5.6 mmol/l or undergoing drug treatment for increased FBG.

Statistical analysis

Continuous variables were presented as the mean (SD), and categorical variables were presented as

percentages. According to their 24-h UAE with normal range (n=2058), study subjects were divided into four groups: Q1, 0–9.38mg/d; Q2, 9.39–11.96 mg/d; Q3, 11.97–15.46 mg/d; and Q4, 11.97–29.99 mg/d.

We performed logistic regression analyses to study the association of MAU and 24-h UAE with MetS and its components, while controlling for covariates including age, sex, education level, regular exercise, alcohol intake and smoking. Participants who were without microalbuminuria or were in the Q1 group were used as a reference group to estimate the odds ratios (ORs) and 95% confidence intervals (CIs). Tests of linear trends across increasing quartiles of 24-h UAE were conducted by treating the medians of the average 24-h UAE as a continuous variable in the logistic regression models. Statistical analyses were performed with SAS 9.3 (SAS Institute Inc.). Tests performed were two-sided, and a *p*-value <0.05 was considered statistically significant.

Patient and public involvement

Patients and/or public were not involved in this study.

RESULTS

Characteristics of subjects

Among the 2261 participants, the prevalence of MAU was 9.0% (203), and prevalence was not statistically significantly different between males and females (8.8% vs. 9.1%, p=0.08). The mean 24-h UAE was 18.0 mg/d. The population's characteristics were summarized according to microalbuminuria and normal range 24-h UAE quartiles in Table 1. Compared to those without MAU, participants with MAU were more likely to have higher WC, BMI, SBP and DBP, FBG and TG. Similarly, these variables were also statistically significant among increasing quartiles of 24-h UAE.

Table 1. General characteristics of the study participants

	Normal range 24-h UAE (mg/d)				*p*-value	Microalbuminuria		*p*-value
	Q1	Q2	Q3	Q4		No	Yes	
Number of subjects	515	515	516	512		2058	203	
Age (years)	41.7(13.5)	42.5(13.5)	41.8(13.5)	42.5(13.3)	0.67	42.1(13.5)	41.4(13.5)	0.48
Men (%)	51.8	48.2	50.8	48.4	0.57	49.8	48.8	0.78
BMI (kg/cm^2)	24.4(3.6)	24.6(3.6)	24.7(3.9)	25.5(3.9)	<0.001	24.8(3.8)	26.0(4.5)	<0.001
WC (cm)	82.3(9.1)	82.4(9.6)	82.7(9.9)	84.8(10.5)	<0.001	83.0(9.8)	85.8(12.5)	<0.001
SBP (mmHg)	129.5(19.4)	130.7(18.5)	129.8(18.7)	133.1(20.7)	0.0111	130.8(19.4)	136.1(23.3)	<0.001
DBP (mmHg)	81.8(11.4)	83.1(10.8)	82.5(11.4)	84.9(12.2)	<0.001	83.1(11.5)	87.9(14.4)	<0.001
High-school (%)	24.1	21.9	23.1	25.4	0.61	23.6	26.6	0.34
Smoking (%)	30.1	29.1	29.1	27.3	0.80	28.9	33.0	0.22
Drinker (%)	23.7	27.6	26.2	27.3	0.47	26.2	27.1	0.78
Regular exercise (%)	17.3	16.7	22.3	22.3	0.03	19.6	30.5	<0.001
FBG (mmol/L)	5.6(1.1)	5.6(1.0)	5.7(1.1)	6.0(1.7)	<0.001	5.7(1.3)	6.5(2.4)	<0.001
TC (mmol/L)	4.7(0.9)	4.8(0.9)	4.8(0.9)	4.9(1.0)	0.0281	4.8(0.9)	5.1(1.0)	<0.001
HDL (mmol/L)	1.3(0.3)	1.3(0.3)	1.3(0.3)	1.2(0.3)	0.0203	1.3(0.3)	1.2(0.3)	0.03
LDL (mmol/L)	2.4(0.7)	2.4(0.6)	2.5(0.7)	2.5(0.7)	0.0186	2.4(0.7)	2.5(0.7)	0.06
TG (mmol/L)	1.4(1.2)	1.4(1.3)	1.5(1.4)	1.8(2.1)	<0.001	1.6(1.6)	2.3(2.4)	<0.001
Creatinine (mmol/d)	6.0(2.2)	7.4(2.6)	8.0(3.2)	8.6(3.1)	<0.001	7.5(3.0)	8.8(3.1)	<0.001
24-h UAE (mg/d)	7.7(1.2)	10.7(0.8)	13.5(1.0)	20.1(3.7)	<0.001	13.0(5.0)	68.8(50.4)	<0.001

MAU and 24-h UAE by the number of MetS components

The prevalence of MAU in MetS and its components are shown in Table 2. The prevalence of MAU was significantly higher for the MetS, high BP, high triglycerides and hyperglycemia groups. The prevalence of MAU for subjects with 0 (n=342), 1 (n=632), 2 (n=632), 3 (n=433), and 4 or 5 (n=222) components of MetS were 5.0, 5.5, 8.2, 14.5 and 16.2%, respectively. The corresponding mean 24-h UAE measurements were 14.5, 15.1, 17.9, 22.7 and 22.8 mg/d. In aggregate, both the prevalence of MAU and the mean 24-h UAE were significantly elevated according to the number of MetS components with all *p*-values <0.001 (Fig 1).

Table 2. Association of microalbuminuria and MetS and its components

Components	Microalbuminuria (%)		*p*-value
	No (n=2058)	Yes (n=203)	
Central obesity			
No	91.49	8.51	0.1982
Yes	89.76	10.24	
High BP			
No	93.52	6.48	<0.001
Yes	88.85	11.15	
High triglycerides			
No	93.11	6.89	<0.001
Yes	86.18	13.82	
Low HDL-C			
No	91.81	8.19	0.0249
Yes	88.72	11.28	
Hyperglycemia			
No	93.94	6.06	<0.0001
Yes	87.78	12.22	
Metabolic syndrome			
No	93.52	6.48	<0.0001
Yes	84.89	15.11	

Association between MAU and MetS components

The association between MAU and the components of MetS are shown in Table 3. Compared with participants without microalbuminuria, the age- and gender-adjusted OR (95% CI) for MetS with microalbuminuria was 2.93 (2.15, 4.00), and the multivariate-adjusted OR (95% CI) was 2.95 (2.15, 4.04). For MetS components, both age- and gender-adjusted and multivariate-adjusted, MAU was strongly associated with high BP, high triglycerides and hyperglycemia. However, no significant association between MAU and central, obesity low HDL-C was found.

Table 3. Relationship between MAU and metabolic syndrome components

	No. of cases	without Microalbuminuria	Microalbuminuria	
			Model 1[a]	Model 2[b]
Metabolic syndrome	655	1.00	2.93(2.15,4.00)	2.95(2.15,4.04)
Central obesity	615	1.00	1.40(0.92,2.13)	1.02(0.65, 1.60)
High BP	1211	1.00	2.20(1.57,3.09)	1.86(1.31, 2.64)
High triglycerides	680	1.00	2.21(1.65,2.97)	1.80(1.31, 2.46)
Low HDL-C	576	1.00	1.71(1.13,2.60)	1.32(0.85, 2.04)
Hyperglycemia	1072	1.00	2.28(1.68,3.11)	1.84(1.34, 2.53)

[a]Model 1: adjusted for age, sex;

[b]Model 2: adjusted for age, sex, education attainment, regular exercise, drinking, smoking and additionally for the other components of the MetS (except for analyses on the MetS).

Associations between high-normal 24-h UAE and MetS

Table 4 revealed that the odd of MetS was gradually elevated according to normal range 24-h UAE quartile. Multivariate-adjusted OR_S of MetS were 1.22, 1.14 and 2.02 for 24-h UAE quartile 2, 3 and 4, compared with the lowest quartile ($p<0.001$). Furthermore, compared to the lowest 24-h UAE quartile, multivariate-adjusted OR of the highest quartile were 1.52 for hyperglycemia (p_{trend} <0.01). However, no significant association between normal range 24-h UAE and the other components of MetS were found.

Table 4. Normal range 24-h UAE quartiles associated with MetS and its components

	Odds Ratio (95% CI)				***p*-Value**
	Q1	**Q2**	**Q3**	**Q4**	
Metabolic syndrome					
Model 1[a]	1.00	1.24 (0.91, 1.67)	1.15 (0.84, 1.56)	2.03 (1.51, 2.72)	<.0001

	Odds Ratio (95% CI)				*p*-Value
	Q1	Q2	Q3	Q4	
Model 2[b]	1.00	1.22 (0.90,1.65)	1.14 (0.84, 1.55)	2.02 (1.51,2.72)	<.0001
Central obesity					
Model 1[a]	1.00	1.35 (0.94, 1.94)	1.07 (0.75, 1.55)	1.72 (1.19, 2.48)	0.0154
Model 2[b]	1.00	1.29 (0.89, 1.88)	1.07 (0.73, 1.58)	1.53 (1.04, 2.25)	0.1221
High BP					
Model 1[a]	1.00	1.18 (0.90, 1.54)	0.99 (0.75, 1.29)	1.43 (1.09, 1.87)	0.0253
Model 2[b]	1.00	1.12 (0.85, 1.48)	0.93 (0.71, 1.23)	1.24 (0.94, 1.64)	0.1957
High triglycerides					
Model 1[a]	1.00	0.96 (0.72, 1.26)	1.00 (0.76, 1.32)	1.43 (1.09, 1.87)	0.0092
Model 2[b]	1.00	0.84 (0.63, 1.13)	0.93(0.69, 1.24)	1.18 (0.89, 1.56)	0.1242
Low HDL-C					
Model 1[a]	1.00	1.37 (0.96, 1.93)	1.28 (0.90, 1.81)	1.55 (1.09, 2.20)	0.0953
Model 2[b]	1.00	1.34 (0.93, 1.94)	1.26 (0.87, 1.83)	1.29 (0.89, 1.87)	0.4045
Hyperglycemia					
Model 1[a]	1.00	1.12 (0.87, 1.44)	1.37 (1.07, 1.77)	1.72 (1.33, 2.21)	0.0001
Model 2[b]	1.00	1.09 (0.84, 1.41)	1.34 (1.03, 1.74)	1.52 (1.17, 1.98)	0.0055

[a]Model 1: adjusted for age, sex;

[b]Model 2: adjusted for age, sex, education attainment, regular exercise, drinking, smoking and additionally for the other components of the MetS (except for analyses on the MetS).

DISCUSSION

Our study showed the prevalence of MAU was 9.0% in the study population and much more prevalent in persons with MetS (15.1%) in particular. The prevalence of MAU in our study was moderate compared with that of other studies in China (4.1–15%) [13-14, 21-24]. This varied prevalence observed in the Chinese population may be associated with different age distribution, region, and method of defining MAU.

In the current study, the prevalence of MAU was consistently higher in persons with MetS than those without MetS. The prevalence of MAU increased significantly with increasing proportions of MetS components after the subjects were divided by the number of MetS components. The same results were obtained in previous studies [12-15, 25–26]. This finding indicates that a large number of participants with MAU are easily overlooked in routine health examinations that do not include MAU measurements. This finding also suggests that intervention for MetS should be started at the earliest stage of renal injury.

Furthermore, our study showed that MAU was significantly associated with MetS and its components apart from central obesity and low HDL-C. Many epidemiologic studies suggested an independent association between MAU and MetS. However, findings on the associations between various components of MetS components and MAU were controversial. Blood pressure and fasting glucose were consistently found to be two main risk factors associated with MAU, which was also clearly shown in our study. However, the association between MAU and abdominal obesity, HDL and triglyceride were inconsistent in previous studies [8, 9, 16]. Thus far, two studies have reported an association between MAU and risk of MetS, with OR (95% CI) of 5.13 (1.96–13.45) and 2.71 (1.69–4.36) [14, 15], consistent with our finding.

Our study further showed that MetS gradually increased with increasing normal range 24-h UAE quartiles, which is consistent with previous studies [15, 26-28]. Thus far, only one prospective cohort study reported hazard ratios with 95% CIs for MetS: 1.57 (1.14–2.18) for the three highest albumin-to-creatinine ratio quartiles compared to the lowest one [28]. However, the association between the components of MetS and high-normal 24-h UAE were not exactly the same. Ge et al. reported that the relationship between 24-h UAE within normal range and central obesity, elevated blood pressure and elevated triglycerides was significant [15]. Another study also found that the association between low-grade albuminuria and the components of MetS was significant except for low HDL-C [25]. In our study,

the relationship between high-normal 24-h UAE and hyperglycemia in the general Chinese population was found. This association persisted after the adjustment for multiple risk factors.

In our study, we found not only MAU but also elevated 24-h UAE within normal range had a significant relationship with increased risk of MetS in Chinese adults. The magnitude of this association persisted after controlling for traditional risk factors. Our finding has important public health implications for preventing MetS [15].

Our study had strengths. First, we used 24-h UAE to define microalbuminuria in a relatively large sample population, which was more accurate than most previous studies in the general Chinese population. Furthermore, our study rigorously conducted standardized methods and quality control for data collection. However, our study had several limitations. First, due to investigative convenience, we did not use an objective biomarker such as para-aminobenzoic acid to assess complete 24-h urine [29]. We assessed the completeness by measuring urinary volume and creatinine concentration in the present study. Second, we did not evaluate the renal function of the subjects, which may cause some bias in the results. Finally, because this study had a cross-sectional design, it was difficult to interpret a causal association between MAU and 24-h UAE with MetS and its components. Therefore, future prospective studies are recommended to confirm our findings.

CONCLUSIONS

Our study confirmed both MAU and high-normal 24-h UAE were stronger risk factors for MetS in the general Chinese population. Assessment of these risk factors can open a window of opportunity for early intervention to decrease the effects of MetS in China.

Acknowledgements Special thanks to Prof. Jixiang Ma for his great contribution to the project initiation. We would such as to express our sincere appreciation to all staff for performing the field work.

We are also grateful to all the study participants.

Contributions JM, XC, JW designed the study and supervised data collection. JX, LY, XC, XG, and YZ participated in field work and data collection. JX and LY analyzed the data. JX wrote the manuscript to which all the authors contributed. JM and JW critically revised the manuscript for important intellectual content. All the authors reviewed and approved the final manuscript.

Funding The survey was supported by Shandong-Ministry of Health Action on Salt Reduction and Hypertension (No.2013) and the Young Scholar Scientific Research Foundation of the Chinese Center for Disease Control and Prevention (No. 2018A203).

Competing interests None declared.

Ethics approval The survey was approved by the Ethics Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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Figure 1. Prevalence of MAU (panel A) and mean 24-h UAE (panel B) according to the number of MetS components.

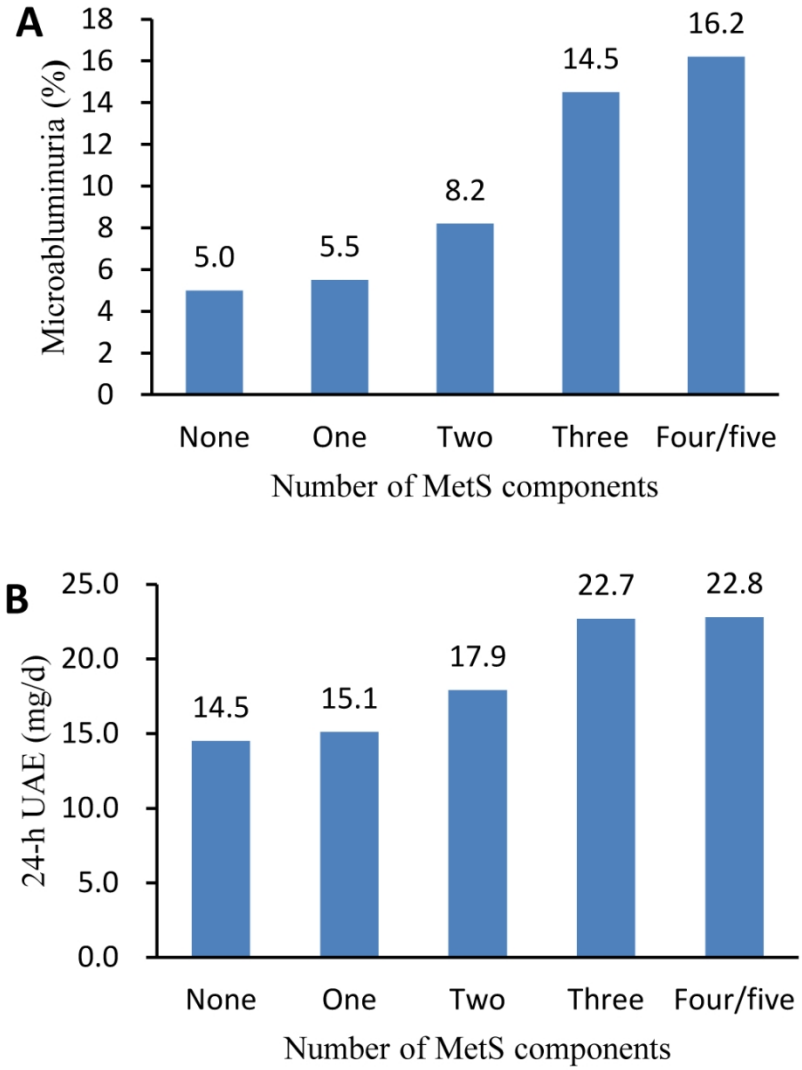

Figure 1. Prevalence of MAU (panel A) and mean 24-h UAE (panel B) according to the number of MetS components.

BMJ Open

Association of microalbuminuria and high-normal 24-hour urinary albumin excretion with metabolic syndrome and its components in the general Chinese population: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031443.R1
Article Type:	Original research
Date Submitted by the Author:	17-Aug-2019
Complete List of Authors:	Xu, Jianwei; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Ma, Jixiang; Chinese Center for Disease Control and Prevention Chen, Xiaorong; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention Yan, Liuxia; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention Cai, Xiaoning; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention Guo, Xiaolei; Shandong Center for Disease Control and Prevention Zhang, Yongqing; Jiangsu Center for Disease Control and Prevention Wu, Jing; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	Metabolic Syndrome, Microalbuminuria, Urinary Albumin

Association of microalbuminuria and high-normal 24-hour urinary albumin excretion with metabolic syndrome and its components in the general Chinese population: a cross-sectional study

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Abstract

Objective: Microalbuminuria has been described as a risk factor for metabolic syndrome (MetS). However, the association between MetS components with microalbuminuria and 24-h urinary albumin excretion (UAE) has not been clearly explained in the general Chinese population. We aimed to analyze the association between microalbuminuria and high-normal 24-h UAE with MetS and its components.

Design: Cross-sectional observational study.

Setting: Four selected counties/districts in China's Shandong and Jiangsu Provinces.

Participants: A total of 2261 participants aged 18-69 years were included in this study. Participants with missing data on physical examination or incomplete urine collection are not included in the analysis.

Results: The prevalence of microalbuminuria was 9.0%, and the mean 24-h UAE was 18.0 mg/d. The prevalence of microalbuminuria was significantly higher for the MetS, high blood pressure, high triglycerides, low high-density lipoprotein cholesterol (HDL-C) and hyperglycemia groups, but not for central obesity. Both microalbuminuria and mean 24-h UAE were significantly increased with a number of MetS components. The adjusted odds ratio (OR) and 95% confidence interval (CI) for MetS with microalbuminuria was 2.95 (2.15 to 4.04) compared to those without microalbuminuria. Microalbuminuria patients were significantly associated with three components of MetS: high blood pressure, high triglycerides and hyperglycemia with OR=1.86, 95% CI 1.31 to 2.64; OR=1.80, 95% CI 1.31 to 2.46; and OR=1.84, 95% CI 1.34 to 2.53, respectively. No significant association of microalbuminuria and central obesity, low HDL-C was found. The presence of MetS were gradually elevated according to the normal range 24-h UAE quartiles: OR=1.00, OR=1.22, OR=1.14 and OR=2.02, respectively. Hyperglycemia was also significantly increased according to the normal range

24-h UAE quartiles.

Conclusions: Microalbuminuria and elevated 24-h UAE within normal range were closely associated with MetS in the Chinese population, which may provide a basis for the development of early intervention to decrease the effects of MetS.

Keywords: Metabolic Syndrome; Microalbuminuria; Urinary Albumin

Strengths and limitations of this study

- We used 24-h UAE to define microalbuminuria, which was more accurate than most previous studies.
- This is the largest sample size of the general Chinese population collected 24-h urine.
- We explore the association between high-normal 24-h UAE with MetS and its components.
- This causal relationship between microalbuminuria and MetS cannot be demonstrated in our cross-sectional study.

INTRODUCTION

Microalbuminuria (MAU), defined by abnormally high albumin excretion (30-300 mg/d) in a 24-h urine sample, was significantly associated with chronic kidney disease, cardiovascular disease and progression of end-stage renal disease independent of traditional risk factors.[1–4] Prospective and epidemiologic studies have found that MAU is also a powerful predictor of all-cause and cardiovascular mortality in the general population. [5-6]

Metabolic syndrome (MetS) is a widely accepted description of a cluster of metabolic abnormalities characterized by obesity, hypertension, dyslipidemia and hyperglycemia. [7] Some

studies have evaluated the relationship between MetS and MAU as a marker for early-stage chronic kidney disease.[8-11] Significant associations between MetS and MAU have been demonstrated in the Japanese, [9] Korean, [10, 12]and Chinese populations. [13-16] However, data concerning the relationship between individual MetS components and MAU were inconsistent, and a causal relationship between MAU and MetS remains unclear despite the predictive value MAU has shown in the aforementioned studies. Furthermore, the study of the association between normal range 24-h urinary albumin excretion (UAE) and MetS components has been limited. [15]

The amount of 24-h UAE is considered the 'gold standard' for defining MAU. [17, 18] However, most of the previous studies of MAU in the Chinese population commonly used an early morning or random spot urine sample instead of measuring 24-h UAE. Therefore, in this study, we investigated the prevalence of MAU by analyzing 24-h UAE and analyzed the association between MAU and normal range 24-h UAE with MetS and its components.

METHODS

Study participants

Data were derived from the supplemental baseline survey of the Shandong Ministry of Health Action on Salt Reduction and Hypertension project, which was a cross-sectional survey conducted at four sites in the Shandong and Jiangsu provinces during 2013 and 2014. We used a stratified, multistage sampling method to select the participants. We selected 80 villages or communities in four sites using proportional probability sampling. Random sample of 120 adults aged 18-69 years were drawn from each villages or communities. A total of 9600 participants were invited to participate in the survey and physical examination. Random sample of at least 30 adults were drawn among 120 adults from each villages or communities. Finally, a subsample of 2408 participants collected a single 24-h urine sample.

Participants with the following conditions were not required to provide urine samples: (1) patients who had difficulty collecting a urine sample; (2) patients with acute and chronic urinary infection; (3) women who were pregnant, breastfeeding, or actively menstruating; and (4) patients with severe vomiting and diarrhea. We excluded 3 subjects with missing data from their physical examination or blood samples and 127 participants with incomplete 24-h urine collection. For the purpose of the present study on microalbuminuria, we also excluded 17 subjects with macroalbuminuria, or a 24-h UAE >300 mg/d. Therefore, a total of 2261 participants were included in this study.

Our study was approved by the ethics committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention (201311). Written informed consent was obtained from all participants.

Demographic, anthropometrical and biochemical data collection

A face-to-face interview was conducted by local trained health professionals using a standard questionnaire. Relevant variables included age, sex, educational level, smoking status, alcohol intake, regular exercise and previous diagnosis and treatment of hypertension and diabetes. During physical examination, height, weight, waist circumference (WC) and blood pressure (BP) were measured by trained researchers using standardized protocols and techniques. Weight and height were measured with participants dressed in light, indoor clothing without shoes by standardized techniques and calibrated equipment. The waist circumference was measured at the narrowest point between the lower border of the rib cage and the iliac crest. The body mass index (BMI) was calculated as the weight in kilograms divided by the height in meters squared (kg/m^2). Blood pressure was measured three times by electronic sphygmomanometer (HEM-7071, Omron Corporation, Japan), and the final blood pressure was obtained by averaging the three measurements.

Fasting blood samples collected from each participant were processed and shipped in cold storage

to a certified laboratory (ADICON Clinical Laboratory Inc., Jinan, China). Fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured. Plasma glucose was measured using a modified hexokinase enzymatic method. Serum cholesterol and triglyceride levels were analyzed enzymatically using commercially available reagents.

24-h Urine collection and analysis

Eligible participants were instructed not to change their dietary and lifestyle habits. We provided a standard plastic container for each participant to collect a 24-h urine sample. Trained researchers gave each participant both written and verbal instructions on how to collect a 24-h urine sample. Health professionals carefully explained to the subjects the purpose of the 24-h urine collection and asked the subjects to correctly repeat the information. The exact 24-h urine collection time, including starting and ending times, was recorded by the supervising health professional. The total volume of the collection was measured by a laboratory technician, and urine aliquots were frozen at −20°C about 30 days and shipped to ADICON Clinical Laboratory in Jinan. Urinary creatinine was measured by the picric acid method. UAE was measured with an immunonephelometric method using the Olympus AU640 Analyzer, for which the coefficient of variation was 3.0%. Either a 24-h urinary volume less than 500 ml or a 24-h urinary creatinine volume that was ±2 standard deviations (SD) outside of the sex-specific mean, 0.98 to 16.17 mmol/l for men and 0.93 to 13.60 mmol/l for women, was defined as an incomplete urine collection. [19]

Definition of the metabolic syndrome

We adopted the harmonized criteria of MetS, which defines MetS as the presence of ≥3 of the following risk factors [20]: central obesity defined as a WC ≥90 cm in men and ≥80 cm in women; high BP defined as a systolic blood pressure (SBP) ≥130 mmHg, a diastolic blood pressure (DBP) ≥85

mmHg or undergoing treatment with an antihypertensive medication; high triglycerides defined as a fasting plasma TC level ≥1.7 mmol/l or drug treatment for increased TC; low HDL-C defined as HDL-C <1.0 mmol/l in men and <1.3 mmol/l in women or drug treatment for increased HDL-C; or hyperglycemia defined as FBG level ≥5.6 mmol/l or undergoing drug treatment for increased FBG.

Statistical analysis

Continuous variables were presented as the mean (SD), and categorical variables were presented as percentages. According to their quartiles of 24-h UAE with normal range (n=2058), study subjects were divided into four groups: Q1, 0–9.38mg/d; Q2, 9.39–11.96 mg/d; Q3, 11.97–15.46 mg/d; and Q4, 15.47–29.99 mg/d.

We performed logistic regression analyses to study the association of MAU and 24-h UAE with MetS and its components, while controlling for covariates including sociodemographic factors (age, sex, education level) and lifestyle factors (regular exercise, alcohol intake and smoking). Participants who were without microalbuminuria or were in the Q1 group were used as a reference group to estimate the odds ratios (ORs) and 95% confidence intervals (CIs). Tests of linear trends across increasing quartiles of 24-h UAE were conducted by treating the medians of the average 24-h UAE as a continuous variable in the logistic regression models. Statistical analyses were performed with SAS 9.3 (SAS Institute Inc.). Tests performed were two-sided, and a *p*-value <0.05 was considered statistically significant.

Patient and public involvement

Patients and the public were not involved in the design or planning of the study.

RESULTS

Characteristics of subjects

Among the 2261 participants, the prevalence of MAU was 9.0% (203), and prevalence was not statistically significantly different between males and females (8.8% vs. 9.1%, p=0.08). The mean 24-h UAE was 18.0 mg/d. The population's characteristics were summarized according to microalbuminuria and normal range 24-h UAE quartiles in Table 1. Compared to those without MAU, participants with MAU were more likely to have higher WC, BMI, SBP and DBP, FBG and TG. Similarly, these variables were also statistically significant among increasing quartiles of 24-h UAE.

Table 1. General characteristics of the study participants

	Normal range 24-h UAE (mg/d)				p-value	Microalbuminuria		p-value
	Q1	Q2	Q3	Q4		No	Yes	
Number of subjects	515	515	516	512		2058	203	
Age (years)	41.7(13.5)	42.5(13.5)	41.8(13.5)	42.5(13.3)	0.67	42.1(13.5)	41.4(13.5)	0.48
Men (%)	51.8	48.2	50.8	48.4	0.57	49.8	48.8	0.78
BMI (kg/cm^2)	24.4(3.6)	24.6(3.6)	24.7(3.9)	25.5(3.9)	<0.001	24.8(3.8)	26.0(4.5)	<0.001
WC (cm)	82.3(9.1)	82.4(9.6)	82.7(9.9)	84.8(10.5)	<0.001	83.0(9.8)	85.8(12.5)	<0.001
SBP (mmHg)	129.5(19.4)	130.7(18.5)	129.8(18.7)	133.1(20.7)	0.0111	130.8(19.4)	136.1(23.3)	<0.001
DBP (mmHg)	81.8(11.4)	83.1(10.8)	82.5(11.4)	84.9(12.2)	<0.001	83.1(11.5)	87.9(14.4)	<0.001
High-school (%)	24.1	21.9	23.1	25.4	0.61	23.6	26.6	0.34
Smoking (%)	30.1	29.1	29.1	27.3	0.80	28.9	33.0	0.22
Drinker (%)	23.7	27.6	26.2	27.3	0.47	26.2	27.1	0.78
Regular exercise (%)	17.3	16.7	22.3	22.3	0.03	19.6	30.5	<0.001
FBG (mmol/L)	5.6(1.1)	5.6(1.0)	5.7(1.1)	6.0(1.7)	<0.001	5.7(1.3)	6.5(2.4)	<0.001
TC (mmol/L)	4.7(0.9)	4.8(0.9)	4.8(0.9)	4.9(1.0)	0.0281	4.8(0.9)	5.1(1.0)	<0.001
HDL (mmol/L)	1.3(0.3)	1.3(0.3)	1.3(0.3)	1.2(0.3)	0.0203	1.3(0.3)	1.2(0.3)	0.03
LDL (mmol/L)	2.4(0.7)	2.4(0.6)	2.5(0.7)	2.5(0.7)	0.0186	2.4(0.7)	2.5(0.7)	0.06
TG (mmol/L)	1.4(1.2)	1.4(1.3)	1.5(1.4)	1.8(2.1)	<0.001	1.6(1.6)	2.3(2.4)	<0.001
Creatinine (mmol/d)	6.0(2.2)	7.4(2.6)	8.0(3.2)	8.6(3.1)	<0.001	7.5(3.0)	8.8(3.1)	<0.001
24-h UAE (mg/d)	7.7(1.2)	10.7(0.8)	13.5(1.0)	20.1(3.7)	<0.001	13.0(5.0)	68.8(50.4)	<0.001

MAU and 24-h UAE by the number of MetS components

The prevalence of MAU in MetS and its components are shown in Table 2. The prevalence of MAU

was significantly higher for the MetS, high BP, high triglycerides and hyperglycemia groups. The prevalence of MAU for subjects with 0 (n=342), 1 (n=632), 2 (n=632), 3 (n=433), and 4 or 5 (n=222) components of MetS were 5.0, 5.5, 8.2, 14.5 and 16.2%, respectively. The corresponding mean 24-h UAE measurements were 14.5, 15.1, 17.9, 22.7 and 22.8 mg/d. In aggregate, both the prevalence of MAU and the mean 24-h UAE were significantly elevated according to the number of MetS components with all *p*-values <0.001 (Fig 1).

Table 2. Association of microalbuminuria and MetS and its components

Components	Microalbuminuria (%)		*p*-value
	No (n=2058)	Yes (n=203)	
Central obesity			
No	91.49	8.51	0.1982
Yes	89.76	10.24	
High BP			
No	93.52	6.48	<0.001
Yes	88.85	11.15	
High triglycerides			
No	93.11	6.89	<0.001
Yes	86.18	13.82	
Low HDL-C			
No	91.81	8.19	0.0249
Yes	88.72	11.28	
Hyperglycemia			
No	93.94	6.06	<0.0001
Yes	87.78	12.22	
Metabolic syndrome			
No	93.52	6.48	<0.0001
Yes	84.89	15.11	

Association between MAU and MetS components

The association between MAU and the components of MetS are shown in Table 3. Compared with participants without microalbuminuria, the age- and gender-adjusted OR (95% CI) for MetS with microalbuminuria was 2.93 (2.15 to 4.00), and the multivariate-adjusted OR (95% CI) was 2.95 (2.15 to 4.04). For MetS components, both age- and gender-adjusted and multivariate-adjusted, MAU was strongly associated with high BP, high triglycerides and hyperglycemia. However, no significant association between MAU and central, obesity low HDL-C was found.

Table 3. Relationship between MAU and metabolic syndrome components

	No. of cases	without Microalbuminuria	Microalbuminuria	
			Model 1[a]	Model 2[b]
Metabolic syndrome	655	1.00	2.93 (2.15 to 4.00)	2.95 (2.15 to 4.04)
Central obesity	615	1.00	1.40 (0.92 to 2.13)	1.02 (0.65 to 1.60)
High BP	1211	1.00	2.20 (1.57 to 3.09)	1.86 (1.31 to 2.64)
High triglycerides	680	1.00	2.21 (1.65 to 2.97)	1.80 (1.31 to 2.46)
Low HDL-C	576	1.00	1.71 (1.13 to 2.60)	1.32 (0.85 to 2.04)
Hyperglycemia	1072	1.00	2.28 (1.68 to 3.11)	1.84 (1.34 to 2.53)

[a]Model 1: adjusted for age, sex;

[b]Model 2: adjusted for age, sex, education attainment, regular exercise, drinking, smoking and additionally for the other components of the MetS (except for analyses on the MetS).

Associations between high-normal 24-h UAE and MetS

Table 4 revealed that the odd of MetS was gradually elevated according to normal range 24-h UAE quartile. Multivariate-adjusted OR_S of MetS were 1.22, 1.14 and 2.02 for 24-h UAE quartile 2, 3 and 4,

compared with the lowest quartile (p<0.0001). Furthermore, compared to the lowest 24-h UAE quartile, multivariate-adjusted OR of the highest quartile were 1.52 for hyperglycemia (p<0.01). However, no significant association between normal range 24-h UAE and the other components of MetS were found.

Table 4. Normal range 24-h UAE quartiles associated with MetS and its components

	Odds Ratio (95% CI)				*p*-Value
	Q1	Q2	Q3	Q4	
Metabolic syndrome					
Model 1[a]	1.00	1.24 (0.91 to 1.67)	1.15 (0.84 to 1.56)	2.03 (1.51 to 2.72)	<0.0001
Model 2[b]	1.00	1.22 (0.90 to 1.65)	1.14 (0.84 to 1.55)	2.02 (1.51 to 2.72)	<0.0001
Central obesity					
Model 1[a]	1.00	1.35 (0.94 to 1.94)	1.07 (0.75 to 1.55)	1.72 (1.19 to 2.48)	0.0154
Model 2[b]	1.00	1.29 (0.89 to 1.88)	1.07 (0.73 to 1.58)	1.53 (1.04 to 2.25)	0.1221
High BP					
Model 1[a]	1.00	1.18 (0.90 to 1.54)	0.99 (0.75 to 1.29)	1.43 (1.09 to 1.87)	0.0253
Model 2[b]	1.00	1.12 (0.85 to 1.48)	0.93 (0.71 to 1.23)	1.24 (0.94 to 1.64)	0.1957
High triglycerides					
Model 1[a]	1.00	0.96 (0.72 to 1.26)	1.00 (0.76 to 1.32)	1.43 (1.09 to 1.87)	0.0092
Model 2[b]	1.00	0.84 (0.63 to 1.13)	0.93(0.69 to 1.24)	1.18 (0.89 to 1.56)	0.1242
Low HDL-C					
Model 1[a]	1.00	1.37 (0.96 to 1.93)	1.28 (0.90 to 1.81)	1.55 (1.09 to 2.20)	0.0953
Model 2[b]	1.00	1.34 (0.93 to 1.94)	1.26 (0.87 to 1.83)	1.29 (0.89 to 1.87)	0.4045
Hyperglycemia					
Model 1[a]	1.00	1.12 (0.87 to 1.44)	1.37 (1.07 to 1.77)	1.72 (1.33 to 2.21)	0.0001
Model 2[b]	1.00	1.09 (0.84 to 1.41)	1.34 (1.03 to 1.74)	1.52 (1.17 to 1.98)	0.0055

[a]Model 1: adjusted for age, sex;

[b]Model 2: adjusted for age, sex, education attainment, regular exercise, drinking, smoking and additionally for the other components of the MetS (except for analyses on the MetS).

DISCUSSION

Our study showed the prevalence of MAU was 9.0% in the study population and much more prevalent in persons with MetS (15.1%) in particular. The prevalence of MAU in our study was moderate compared with that of other studies in China (4.1% to 15%).[13-14, 21-24] This varied prevalence observed in the Chinese population may be associated with different age distribution, region, and method of defining MAU.

In the current study, the prevalence of MAU was consistently higher in persons with MetS than those without MetS. The prevalence of MAU increased significantly with increasing proportions of MetS components after the subjects were divided by the number of MetS components. The same results were obtained in previous studies. [12-15, 25–26] This finding indicates that a large number of participants with MAU are easily overlooked in routine health examinations that do not include MAU measurements. This finding also suggests that intervention for MetS should be started at the earliest stage of renal injury.

Furthermore, our study showed that MAU was significantly associated with MetS and its components apart from central obesity and low HDL-C. Many epidemiologic studies suggested an independent association between MAU and MetS. However, findings on the associations between various components of MetS components and MAU were controversial. Blood pressure and fasting glucose were consistently found to be two main risk factors associated with MAU, which was also clearly shown in our study. However, the association between MAU and abdominal obesity, HDL and triglyceride were inconsistent in previous studies. [8, 9, 16] Thus far, two studies have reported an association between MAU and risk of MetS, with OR (95% CI) of 5.13 (1.96 to 13.45) and 2.71 (1.69 to 4.36), [14, 15] consistent with our finding.

Our study further showed that MetS gradually increased with increasing normal range 24-h UAE quartiles, which is consistent with previous studies. [15, 26-28] Thus far, only one prospective cohort

study reported hazard ratios with 95% CIs for MetS: 1.57 (1.14 to 2.18) for the three highest albumin-to-creatinine ratio quartiles compared to the lowest one. [28] However, the association between the components of MetS and high-normal 24-h UAE were not exactly the same. Ge et al. reported that the relationship between 24-h UAE within normal range and central obesity, elevated blood pressure and elevated triglycerides was significant. [15] Another study also found that the association between low-grade albuminuria and the components of MetS was significant except for low HDL-C. [25] In our study, the relationship between high-normal 24-h UAE and hyperglycemia in the general Chinese population was found. This association persisted after the adjustment for multiple risk factors.

In our study, we found not only MAU but also elevated 24-h UAE within normal range had a significant relationship with increased risk of MetS in Chinese adults. The magnitude of this association persisted after controlling for traditional risk factors. Our finding has important public health implications for preventing MetS. [15] The prevalence of MetS in China was 24.2%, [29] which is becoming a serious public health problem in China. Our findings demonstrated that the lowering of 24 h UAE even within normal range should be an important priority for reducing the effects of MetS. Our study suggested clinicians should carefully evaluate the risk of MetS with normal rang UAE. Annual MAU screening in MetS population should be an essential part of our preventive medicine efforts. Policy makers should support such screening as part of the universal coverage policy programs.

Our study had strengths. First, we used 24-h UAE to define microalbuminuria in a relatively large sample population, which was more accurate than most previous studies in the general Chinese population. Furthermore, it is a population-based epidemiologic study found the association between high-normal 24-h UAE and Mets, which is the difference from most previous studies in China. In addition, our study rigorously conducted standardized methods and quality control for data

collection. However, our study had several limitations. First, due to investigative convenience, we did not use an objective biomarker such as para-aminobenzoic acid to assess complete 24-h urine. [30] We assessed the completeness by measuring urinary volume and creatinine concentration in the present study. Second, we did not evaluate the renal function of the subjects, which may cause some bias in the results. Third, although multiple covariates had been included in the adjustment, some potential confounding factors, such as dietary intake, [31] other medications could not be ruled out. Finally, because this study had a cross-sectional design, it was difficult to interpret a causal association between MAU and 24-h UAE with MetS and its components. Therefore, future prospective studies are recommended to confirm our findings.

CONCLUSIONS

Our study confirmed both MAU and high-normal 24-h UAE were stronger risk factors for MetS in the general Chinese population. Assessment of these risk factors can open a window of opportunity for early intervention to decrease the effects of MetS in China.

Acknowledgements Special thanks to Prof. Jixiang Ma for his great contribution to the project initiation. We would such as to express our sincere appreciation to all staff for performing the field work. We are also grateful to all the study participants.

Contributions JM, XC, JW designed the study and supervised data collection. JX, LY, XC, XG, and YZ participated in field work and data collection. JX and LY analyzed the data. JX wrote the manuscript to which all the authors contributed. JM and JW critically revised the manuscript for important intellectual content. All the authors reviewed and approved the final manuscript.

Funding The survey was supported by Shandong-Ministry of Health Action on Salt Reduction and Hypertension (No.2013) and the Young Scholar Scientific Research Foundation of the Chinese Center

for Disease Control and Prevention (No. 2018A203).

Competing interests None declared.

Ethics approval The survey was approved by the Ethics Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement A de-identified minimal data set that underlies the findings and conclusions described in the manuscript can be shared upon request by the editors to verify the reported study findings.

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Figure 1. Prevalence of MAU (panel A) and mean 24-h UAE (panel B) according to the number of MetS components.

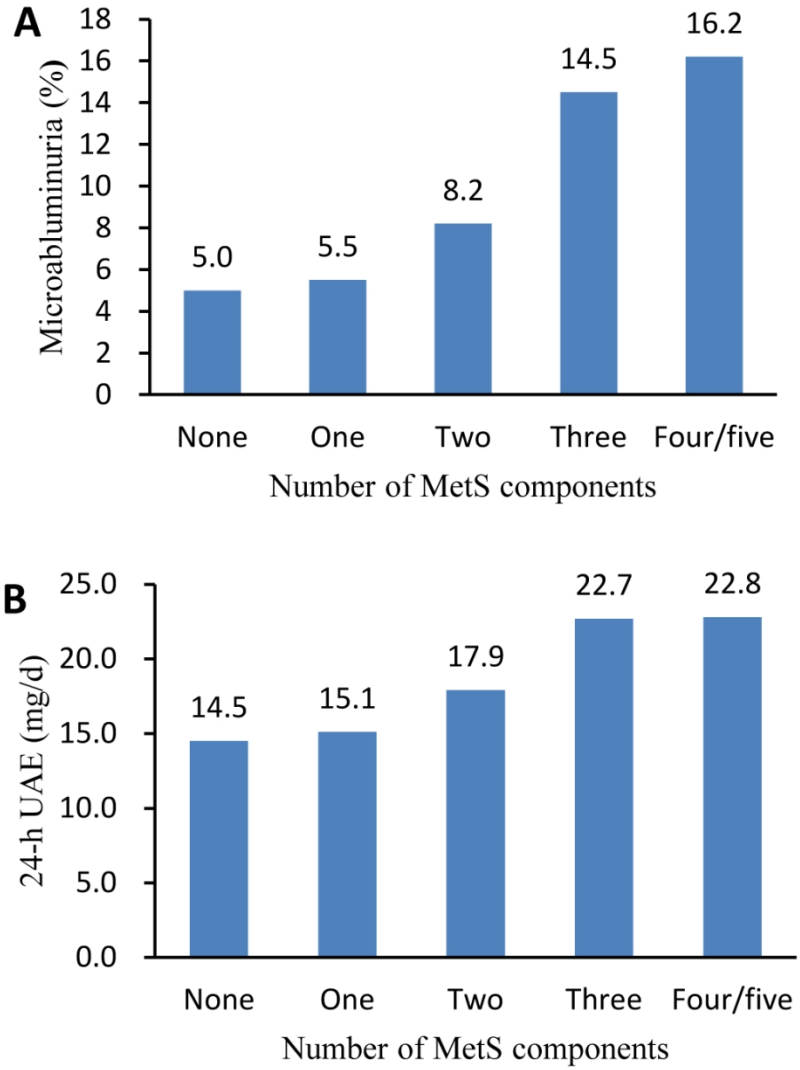

Figure 1. Prevalence of MAU (panel A) and mean 24-h UAE (panel B) according to the number of MetS components.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **[1]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[3-4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[4]**
Methods		
Study design	4	Present key elements of study design early in the paper **[4]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[4]**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **[4-5]**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[5-7]**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **[5-7]**
Bias	9	Describe any efforts to address potential sources of bias **[7]**
Study size	10	Explain how the study size was arrived at **[4-5]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[5]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[7]**
		(*b*) Describe any methods used to examine subgroups and interactions **[7]**
		(*c*) Explain how missing data were addressed **[5]**
		(*d*) If applicable, describe analytical methods taking account of sampling strategy **[N/A]**
		(*e*) Describe any sensitivity analyses **[N/A]**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **[8]**
		(b) Give reasons for non-participation at each stage **[5]**
		(c) Consider use of a flow diagram **[N/A]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[8-9]**
		(b) Indicate number of participants with missing data for each variable of interest **[8]**
Outcome data	15*	Report numbers of outcome events or summary measures **[9]**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **[10]**
		(*b*) Report category boundaries when continuous variables were categorized **[7,11]**

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[N/A]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[11]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[11-12]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[13-14]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence**[13]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[13]**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **[14]**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Association of microalbuminuria and high-normal 24-hour urinary albumin excretion with metabolic syndrome and its components in the general Chinese population: a cross-sectional study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-031443.R2
Article Type:	Original research
Date Submitted by the Author:	30-Sep-2019
Complete List of Authors:	Xu, Jianwei; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Ma, Jixiang; Chinese Center for Disease Control and Prevention Chen, Xiaorong; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention Yan, Liuxia; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention Cai, Xiaoning; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention Guo, Xiaolei; Shandong Center for Disease Control and Prevention Zhang, Yongqing; Jiangsu Center for Disease Control and Prevention Wu, Jing; National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	Metabolic Syndrome, Microalbuminuria, Urinary Albumin

Association of microalbuminuria and high-normal 24-hour urinary albumin excretion with metabolic syndrome and its components in the general Chinese population: a cross-sectional study

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Abstract

Objective: Microalbuminuria has been described as a risk factor for metabolic syndrome (MetS). However, the association of MetS components with microalbuminuria and 24-h urinary albumin excretion (UAE) has not been clearly explained in the general Chinese population. We aimed to analyse the associations of microalbuminuria and high-normal 24-h UAE with MetS and its components.

Design: Cross-sectional observational study.

Setting: Four selected counties/districts in China's Shandong and Jiangsu Provinces.

Participants: A total of 2261 participants aged 18-69 years were included in this study. Participants with missing physical examination data or incomplete urine collection were not included in the analysis.

Results: The prevalence of microalbuminuria was 9.0%, and the mean 24-h UAE was 18.0 mg/d. The prevalence of microalbuminuria was significantly higher for the MetS, high blood pressure, high triglycerides, low high-density lipoprotein cholesterol (HDL-C) and hyperglycaemia groups but not for the central obesity group. Both microalbuminuria and mean 24-h UAE were significantly increased in association with a number of MetS components. The adjusted prevalence odds ratio (POR) and 95% confidence interval (CI) for MetS with microalbuminuria was 2.95 (2.15 to 4.04) compared to those without microalbuminuria. Microalbuminuria was significantly associated with three components of MetS: high blood pressure, high triglycerides and hyperglycaemia (POR=1.86, 95% CI 1.31 to 2.64; POR=1.80, 95% CI 1.31 to 2.46; and POR=1.84, 95% CI 1.34 to 2.53, respectively). No significant association of microalbuminuria with central obesity or low HDL-C was found. The presence of MetS gradually increased according to the normal-range 24-h UAE quartiles: POR=1.00, POR=1.22, POR=1.14 and POR=2.02, respectively. Hyperglycaemia also increased significantly according to the normal-range 24-h UAE quartiles.

Conclusions: Microalbuminuria and elevated 24-h UAE within the normal range were closely associated

with MetS in the Chinese population, which may provide a basis for the development of early interventions to decrease the effects of MetS.

Keywords: Metabolic Syndrome; Microalbuminuria; Urinary Albumin

Strengths and limitations of this study

- We used 24-h UAE to define microalbuminuria, which is more accurate than most previous studies.
- This is the largest sample size of the general Chinese population to collected 24-h urine.
- We explored the association between high-normal 24-h UAE with MetS and its components.
- A causal relationship between microalbuminuria and MetS cannot be demonstrated in our cross-sectional study.

INTRODUCTION

Microalbuminuria (MAU), defined by abnormally high albumin excretion (30-300 mg/d) in a 24-h urine sample, was significantly associated with chronic kidney disease, cardiovascular disease and progression of end-stage renal disease independent of traditional risk factors.[1-4] Prospective and epidemiologic studies have found that MAU is also a powerful predictor of all-cause and cardiovascular mortality in the general population. [5-6]

Metabolic syndrome (MetS) is a widely accepted description of a cluster of metabolic abnormalities characterized by obesity, hypertension, dyslipidaemia and hyperglycaemia. [7] Some studies have evaluated the relationship between MetS and MAU as a marker for early-stage chronic kidney disease.[8-11] Significant associations between MetS and MAU have been demonstrated in Japanese, [9] Korean, [10, 12] and Chinese populations. [13-16] However, data concerning the relationship between individual

MetS components and MAU have been inconsistent, and a causal relationship between MAU and MetS remains unclear despite the predictive value MAU showed in the aforementioned studies. Furthermore, the study of the association between normal-range 24-h urinary albumin excretion (UAE) and MetS components has been limited. [15]

The 24-h UAE level is considered the 'gold standard' for defining MAU. [17, 18] However, most of the previous studies of MAU in the Chinese population have used an early morning or random spot urine sample instead of measuring 24-h UAE. Therefore, in this study, we investigated the prevalence of MAU by analysing 24-h UAE and analysed the association of MAU and normal-range 24-h UAE with MetS and its components.

METHODS

Study participants

Data were derived from the supplemental baseline survey of the Shandong Ministry of Health Action on Salt Reduction and Hypertension project, which was a cross-sectional survey conducted at four sites in the Shandong and Jiangsu provinces during 2013 and 2014. We used a stratified, multistage sampling method to select the participants. We selected 80 villages or communities from four sites using proportional probability sampling. A random sample of 120 adults aged 18-69 years was drawn from each village or community. A total of 9600 people were selected, and 8995 of these individuals participated in the survey (response rate, 93.7%). A total of 605 replacements were selected from all individuals in the same village or community after excluding the already selected participants. A total of 9600 individuals participated in the survey and physical examination. A random sample of at least 30 adults was drawn among 120 adults from each village or community. A total of 2480 people were selected, and 2295 participated in the survey (response rate, 92.5%). Of the 185 nonresponders, 113 were replaced

by adults with similar profiles from the same community or village. Finally, a subsample of 2408 participants collected a single 24-h urine sample. Participants with the following conditions were not required to provide urine samples: (1) patients who had difficulty collecting a urine sample; (2) patients with an acute or chronic urinary infection; (3) women who were pregnant, breastfeeding, or actively menstruating; and (4) patients with severe vomiting or diarrhoea. We excluded 3 subjects with missing data from their physical examination or blood samples and 127 participants with incomplete 24-h urine collection. For the purpose of the present study on microalbuminuria, we also excluded 17 subjects with macroalbuminuria or a 24-h UAE >300 mg/d. Therefore, a total of 2261 participants were included in this study.

Our study was approved by the ethics committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention (201311). Written informed consent was obtained from all participants.

Demographic, anthropometrical and biochemical data collection

A face-to-face interview was conducted by local trained health professionals using a standard questionnaire. Relevant variables included age, sex, educational level, smoking status, alcohol intake, regular exercise and previous diagnosis and treatment of hypertension and diabetes. During the physical examination, height, weight, waist circumference (WC) and blood pressure (BP) were measured by trained researchers using standardized protocols and techniques. Weight and height were measured with participants dressed in light, indoor clothing without shoes using standardized techniques and calibrated equipment. Waist circumference was measured at the narrowest point between the lower border of the rib cage and the iliac crest. The body mass index (BMI) was calculated as the weight in kilograms divided by the height in metres squared (kg/m^2). Blood pressure was measured three times by an electronic sphygmomanometer (HEM-7071, Omron Corporation, Japan), and the final blood pressure was obtained

by averaging the three measurements.

Fasting blood samples collected from each participant were processed and shipped in cold storage to a certified laboratory (ADICON Clinical Laboratory Inc., Jinan, China). Fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured. Plasma glucose was measured using a modified hexokinase enzymatic method. Serum cholesterol and triglyceride levels were analysed enzymatically using commercially available reagents.

24-h Urine collection and analysis

Eligible participants were instructed not to change their dietary or lifestyle habits. We provided a standard plastic container for each participant to collect a 24-h urine sample. Trained researchers gave each participant both written and verbal instructions on how to collect a 24-h urine sample. Health professionals carefully explained to the subjects the purpose of the 24-h urine collection and asked the subjects to correctly repeat the information. The exact 24-h urine collection time, including starting and ending times, was recorded by the supervising health professional. The total volume of the collection was measured by a laboratory technician, and urine aliquots were frozen at −20°C for approximately 30 days and shipped to the ADICON Clinical Laboratory in Jinan. Urinary creatinine was measured by the picric acid method. UAE was measured with an immunonephelometric method using the Olympus AU640 Analyser, for which the coefficient of variation was 3.0%. Either a 24-h urinary volume less than 500 ml or a 24-h urinary creatinine volume that was ±2 standard deviations (SD) outside of the sex-specific mean, 0.98 to 16.17 mmol/l for men and 0.93 to 13.60 mmol/l for women, was defined as an incomplete urine collection. [19]

Definition of metabolic syndrome

We adopted the harmonized criteria of MetS, which defines MetS as the presence of ≥3 of the following

risk factors [20]: central obesity defined as a WC ≥90 cm in men and ≥80 cm in women; high BP defined as a systolic blood pressure (SBP) ≥130 mmHg, a diastolic blood pressure (DBP) ≥85 mmHg or treatment with an antihypertensive medication; high triglycerides defined as a fasting plasma TC level ≥1.7 mmol/l or drug treatment for increased TC; low HDL-C defined as HDL-C <1.0 mmol/l in men and <1.3 mmol/l in women or drug treatment for low HDL-C; and hyperglycaemia defined as a FBG level ≥5.6 mmol/l or drug treatment for increased FBG.

Statistical analysis

Continuous variables are presented as the mean (SD), and categorical variables are presented as percentages. According to their quartiles of 24-h UAE in a normal range (n=2058), study subjects were divided into four groups: Q1, 0–9.38 mg/d; Q2, 9.39–11.96 mg/d; Q3, 11.97–15.46 mg/d; and Q4, 15.47–29.99 mg/d.

We performed logistic regression analyses to study the association of MAU and 24-h UAE with MetS and its components while controlling for covariates including sociodemographic factors (age, sex, education level) and lifestyle factors (regular exercise, alcohol intake and smoking). Participants who did not have microalbuminuria or who were in the Q1 group were used as a reference group to estimate the prevalence odds ratios (PORs) and 95% confidence intervals (CIs). Tests of linear trends across increasing quartiles of 24-h UAE were conducted by treating the medians of the average 24-h UAE as a continuous variable in the logistic regression models. Statistical analyses were performed with SAS 9.3 (SAS Institute Inc.). The tests performed were two-sided, and a *p*-value <0.05 was considered statistically significant.

Patient and public involvement

Patients and the public were not involved in the design or planning of the study.

RESULTS

Characteristics of subjects

Among the 2261 participants, the prevalence of MAU was 9.0% (203), and the prevalence was not significantly different between males and females (8.8% vs. 9.1%, p=0.08). The mean 24-h UAE was 18.0 mg/d. The population characteristics are summarized according to microalbuminuria and normal-range 24-h UAE quartiles in Table 1. Compared to those without MAU, participants with MAU were more likely to have higher WC, BMI, SBP, DBP, FBG and TG. Similarly, these variables were also significantly different among increasing quartiles of 24-h UAE.

Table 1. General characteristics of the study participants

	Normal range 24-h UAE (mg/d)				p-value	Microalbuminuria		p-value
	Q1	Q2	Q3	Q4		No	Yes	
Number of subjects	515	515	516	512		2058	203	
Age (years)	41.7(13.5)	42.5(13.5)	41.8(13.5)	42.5(13.3)	0.67	42.1(13.5)	41.4(13.5)	0.48
Men (%)	51.8	48.2	50.8	48.4	0.57	49.8	48.8	0.78
BMI (kg/cm^2)	24.4(3.6)	24.6(3.6)	24.7(3.9)	25.5(3.9)	<0.001	24.8(3.8)	26.0(4.5)	<0.001
WC (cm)	82.3(9.1)	82.4(9.6)	82.7(9.9)	84.8(10.5)	<0.001	83.0(9.8)	85.8(12.5)	<0.001
SBP (mmHg)	129.5(19.4)	130.7(18.5)	129.8(18.7)	133.1(20.7)	0.0111	130.8(19.4)	136.1(23.3)	<0.001
DBP (mmHg)	81.8(11.4)	83.1(10.8)	82.5(11.4)	84.9(12.2)	<0.001	83.1(11.5)	87.9(14.4)	<0.001
High-school (%)	24.1	21.9	23.1	25.4	0.61	23.6	26.6	0.34
Smoking (%)	30.1	29.1	29.1	27.3	0.80	28.9	33.0	0.22
Alcohol (%)	23.7	27.6	26.2	27.3	0.47	26.2	27.1	0.78
Regular exercise (%)	17.3	16.7	22.3	22.3	0.03	19.6	30.5	<0.001
FBG (mmol/L)	5.6(1.1)	5.6(1.0)	5.7(1.1)	6.0(1.7)	<0.001	5.7(1.3)	6.5(2.4)	<0.001
TC (mmol/L)	4.7(0.9)	4.8(0.9)	4.8(0.9)	4.9(1.0)	0.0281	4.8(0.9)	5.1(1.0)	<0.001
HDL (mmol/L)	1.3(0.3)	1.3(0.3)	1.3(0.3)	1.2(0.3)	0.0203	1.3(0.3)	1.2(0.3)	0.03
LDL (mmol/L)	2.4(0.7)	2.4(0.6)	2.5(0.7)	2.5(0.7)	0.0186	2.4(0.7)	2.5(0.7)	0.06
TG (mmol/L)	1.4(1.2)	1.4(1.3)	1.5(1.4)	1.8(2.1)	<0.001	1.6(1.6)	2.3(2.4)	<0.001
Creatinine (mmol/d)	6.0(2.2)	7.4(2.6)	8.0(3.2)	8.6(3.1)	<0.001	7.5(3.0)	8.8(3.1)	<0.001
24-h UAE (mg/d)	7.7(1.2)	10.7(0.8)	13.5(1.0)	20.1(3.7)	<0.001	13.0(5.0)	68.8(50.4)	<0.001

MAU and 24-h UAE by the number of MetS components

The prevalence of MAU in individuals with MetS and its components is shown in Table 2. The prevalence of MAU was significantly higher in the MetS, high BP, high triglycerides and hyperglycaemia groups. The prevalence of MAU among subjects with 0 (n=342), 1 (n=632), 2 (n=632), 3 (n=433), and 4 or 5 (n=222) components of MetS was 5.0, 5.5, 8.2, 14.5 and 16.2%, respectively. The corresponding mean 24-h UAE measurements were 14.5, 15.1, 17.9, 22.7 and 22.8 mg/d, respectively. Overall, both the prevalence of MAU and the mean 24-h UAE were significantly elevated according to the number of MetS components with all *p*-values <0.001 (Fig 1).

Table 2. Association of microalbuminuria with MetS and its components

Components	Microalbuminuria (%)		*p*-value
	No (n=2058)	Yes (n=203)	
Central obesity			
No	91.49	8.51	0.1982
Yes	89.76	10.24	
High BP			
No	93.52	6.48	<0.001
Yes	88.85	11.15	
High triglycerides			
No	93.11	6.89	<0.001
Yes	86.18	13.82	
Low HDL-C			
No	91.81	8.19	0.0249
Yes	88.72	11.28	
Hyperglycaemia			
No	93.94	6.06	<0.0001
Yes	87.78	12.22	
Metabolic syndrome			

No	93.52	6.48	<0.0001
Yes	84.89	15.11	

Association between MAU and MetS components

The associations between MAU and the components of MetS are shown in Table 3. Compared with participants without microalbuminuria, the age- and sex-adjusted POR (95% CI) for MetS with microalbuminuria was 2.93 (2.15 to 4.00), and the multivariate-adjusted POR (95% CI) was 2.95 (2.15 to 4.04). For MetS components, in both the age- and sex-adjusted and multivariate-adjusted models, MAU was strongly associated with high BP, high triglycerides and hyperglycaemia. However, no significant association between MAU and central obesity or low HDL-C was found.

Table 3. Relationship between MAU and metabolic syndrome components

	No. of cases	Without microalbuminuria	Microalbuminuria	
			Model 1[a]	Model 2[b]
Metabolic syndrome	655	1.00	2.93 (2.15 to 4.00)	2.95 (2.15 to 4.04)
Central obesity	615	1.00	1.40 (0.92 to 2.13)	1.02 (0.65 to 1.60)
High BP	1211	1.00	2.20 (1.57 to 3.09)	1.86 (1.31 to 2.64)
High triglycerides	680	1.00	2.21 (1.65 to 2.97)	1.80 (1.31 to 2.46)
Low HDL-C	576	1.00	1.71 (1.13 to 2.60)	1.32 (0.85 to 2.04)
Hyperglycaemia	1072	1.00	2.28 (1.68 to 3.11)	1.84 (1.34 to 2.53)

[a]Model 1: adjusted for age and sex;

[b]Model 2: adjusted for age, sex, education attainment, regular exercise, alcohol consumption, smoking and for the other components of MetS (except for analyses of MetS).

Associations between high-normal 24-h UAE and MetS

Table 4 shows that the odds of MetS gradually increased according to the normal-range 24-h UAE quartiles. The multivariate-adjusted PORs of MetS were 1.22, 1.14 and 2.02 for 24-h UAE quartiles 2, 3 and 4, respectively, compared with the lowest quartile ($p<0.0001$). Furthermore, compared to the lowest 24-h UAE quartile, the multivariate-adjusted POR of the highest quartile was 1.52 for hyperglycaemia ($p<0.01$). However, no significant associations between normal-range 24-h UAE and the other components of MetS were found.

Table 4. Normal-range 24-h UAE quartiles associated with MetS and its components

	Prevalence Odds Ratio (95% CI)				*p*-Value
	Q1	Q2	Q3	Q4	
Metabolic syndrome					
Model 1[a]	1.00	1.24 (0.91 to 1.67)	1.15 (0.84 to 1.56)	2.03 (1.51 to 2.72)	<0.0001
Model 2[b]	1.00	1.22 (0.90 to 1.65)	1.14 (0.84 to 1.55)	2.02 (1.51 to 2.72)	<0.0001
Central obesity					
Model 1[a]	1.00	1.35 (0.94 to 1.94)	1.07 (0.75 to 1.55)	1.72 (1.19 to 2.48)	0.0154
Model 2[b]	1.00	1.29 (0.89 to 1.88)	1.07 (0.73 to 1.58)	1.53 (1.04 to 2.25)	0.1221
High BP					
Model 1[a]	1.00	1.18 (0.90 to 1.54)	0.99 (0.75 to 1.29)	1.43 (1.09 to 1.87)	0.0253
Model 2[b]	1.00	1.12 (0.85 to 1.48)	0.93 (0.71 to 1.23)	1.24 (0.94 to 1.64)	0.1957
High triglycerides					
Model 1[a]	1.00	0.96 (0.72 to 1.26)	1.00 (0.76 to 1.32)	1.43 (1.09 to 1.87)	0.0092
Model 2[b]	1.00	0.84 (0.63 to 1.13)	0.93(0.69 to 1.24)	1.18 (0.89 to 1.56)	0.1242
Low HDL-C					
Model 1[a]	1.00	1.37 (0.96 to 1.93)	1.28 (0.90 to 1.81)	1.55 (1.09 to 2.20)	0.0953
Model 2[b]	1.00	1.34 (0.93 to 1.94)	1.26 (0.87 to 1.83)	1.29 (0.89 to 1.87)	0.4045
Hyperglycaemia					
Model 1[a]	1.00	1.12 (0.87 to 1.44)	1.37 (1.07 to 1.77)	1.72 (1.33 to 2.21)	0.0001
Model 2[b]	1.00	1.09 (0.84 to 1.41)	1.34 (1.03 to 1.74)	1.52 (1.17 to 1.98)	0.0055

[a]Model 1: adjusted for age and sex;

[b]Model 2: adjusted for age, sex, education attainment, regular exercise, alcohol consumption, smoking and for the other components of MetS (except for the analyses of MetS).

DISCUSSION

Our study showed that the prevalence of MAU was 9.0% in the study population and was much more prevalent in persons with MetS (15.1%) in particular. The prevalence of MAU in our study was moderate compared with that in other studies in China (4.1% to 15%). [13-14, 21-24] This varied prevalence observed in the Chinese population may be associated with different age distributions, regions, and methods of defining MAU.

In the current study, the prevalence of MAU was consistently higher in persons with MetS than in those without MetS. The prevalence of MAU increased significantly with increasing numbers of MetS components after the subjects were divided by the number of MetS components. The same results were obtained in previous studies. [12-15, 25–26] This finding indicates that a large number of participants with MAU are easily overlooked in routine health examinations that do not include MAU measurements. This finding also suggests that intervention for MetS should be initiated at the earliest stage of renal injury.

Furthermore, our study showed that MAU was significantly associated with MetS and its components, apart from central obesity and low HDL-C. Many epidemiologic studies have suggested an independent association between MAU and MetS. However, findings on the associations between various components of MetS and MAU are controversial. Blood pressure and fasting glucose were consistently found to be two main risk factors associated with MAU, which was also clearly shown in our study. However, the associations between MAU and abdominal obesity, HDL and triglycerides were inconsistent in previous studies. [8, 9, 16] Thus far, two studies have reported an association between

MAU and risk of MetS, with ORs (95% CI) of 5.13 (1.96 to 13.45) and 2.71 (1.69 to 4.36), [14, 15] which is consistent with our finding.

Our study further showed that the prevalence of MetS gradually increased with increasing normal-range 24-h UAE quartiles, which is consistent with previous studies. [15, 26-28] Thus far, only one prospective cohort study reported hazard ratios with 95% CIs for MetS: 1.57 (1.14 to 2.18) for the three highest albumin-to-creatinine ratio quartiles compared to the lowest one. [28] However, the association between the components of MetS and high-normal 24-h UAE were not exactly the same. Ge et al. reported that the relationship between 24-h UAE within the normal range and central obesity, elevated blood pressure and elevated triglycerides was significant. [15] Another study also found that the association between low-grade albuminuria and the components of MetS, except for low HDL-C, was significant. [25] In our study, a relationship between high-normal 24-h UAE and hyperglycaemia in the general Chinese population was found. This association persisted after adjustment for multiple risk factors.

In our study, we found that not only MAU but also elevated 24-h UAE within the normal range had a significant relationship with an increased risk of MetS in Chinese adults. The magnitude of this association persisted after controlling for traditional risk factors. Our finding has important public health implications for preventing MetS. [15] The prevalence of MetS in China was 24.2% [29] and is becoming a serious public health problem in China. Our findings demonstrated that reducing 24 h UAE even within the normal range should be an important priority for reducing the effects of MetS. Our study suggested that clinicians should carefully evaluate the risk of MetS in individuals with normal-range UAE. Annual MAU screening in the MetS population should be an essential part of our preventive medicine efforts. Policy makers should support such screening as part of the universal coverage policy programmes.

Our study had strengths. First, we used 24-h UAE to define microalbuminuria in a relatively large sample population, which was more accurate than most previous studies in the general Chinese population. Furthermore, this population-based epidemiologic study found an association between high-normal 24-h UAE and MetS, which is different from most previous studies in China. In addition, our study rigorously used standardized methods and quality control for data collection. However, our study had several limitations. First, due to investigative convenience, we did not use an objective biomarker, such as para-aminobenzoic acid, to assess complete 24-h urine. [30] We assessed the completeness by measuring urinary volume and creatinine concentration in the present study. Second, we did not evaluate the renal function of the subjects, which may have caused some bias in the results. Third, although multiple covariates were included in the adjustment, some potential confounding factors, such as dietary intake [31] and other medications could not be ruled out. Finally, because this study had a cross-sectional design, it was difficult to interpret a causal association between MAU and 24-h UAE with MetS and its components. Therefore, future prospective studies are recommended to confirm our findings.

CONCLUSIONS

Our study confirmed that both MAU and high-normal 24-h UAE were strong risk factors for MetS in the general Chinese population. The assessment of these risk factors can result in an opportunity for early intervention to decrease the effects of MetS in China.

Acknowledgements Special thanks to Prof. Jixiang Ma for his great contribution to the project initiation. We would like to express our sincere appreciation to all staff for performing the field work. We are also grateful to all the study participants.

Contributions JM, XChen, JW designed the study and supervised data collection. JX, LY, XCai, XG, and YZ participated in field work and data collection. JX and LY analysed the data. JX wrote the

manuscript to which all the authors contributed. JM and JW critically revised the manuscript for important intellectual content. All the authors reviewed and approved the final manuscript.

Funding The survey was supported by Shandong-Ministry of Health Action on Salt Reduction and Hypertension (No. 2013) and the Young Scholar Scientific Research Foundation of the Chinese Center for Disease Control and Prevention (No. 2018A203).

Competing interests None declared.

Ethics approval The survey was approved by the Ethics Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement A de-identified minimal data set that underlies the findings and conclusions described in the manuscript can be shared upon request by the editors to verify the reported study findings.

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Figure 1. Prevalence of MAU (panel A) and mean 24-h UAE (panel B) according to the number of MetS components.

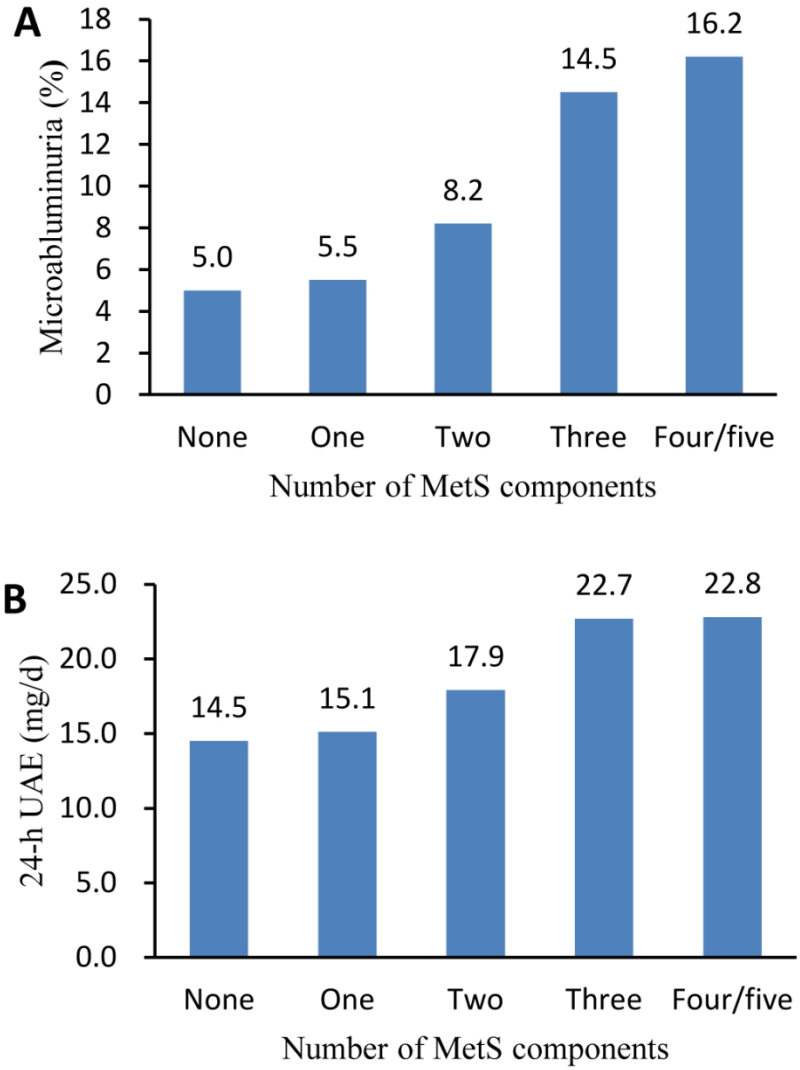

Figure 1. Prevalence of MAU (panel A) and mean 24-h UAE (panel B) according to the number of MetS components.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract **[1]**
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found **[2]**
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported **[3-4]**
Objectives	3	State specific objectives, including any prespecified hypotheses **[4]**
Methods		
Study design	4	Present key elements of study design early in the paper **[4]**
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection **[4]**
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants **[4-5]**
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable **[5-7]**
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group **[5-7]**
Bias	9	Describe any efforts to address potential sources of bias **[7]**
Study size	10	Explain how the study size was arrived at **[4-5]**
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why **[5]**
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding **[7]**
		(*b*) Describe any methods used to examine subgroups and interactions **[7]**
		(*c*) Explain how missing data were addressed **[5]**
		(*d*) If applicable, describe analytical methods taking account of sampling strategy **[N/A]**
		(*e*) Describe any sensitivity analyses **[N/A]**
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed **[8]**
		(b) Give reasons for non-participation at each stage **[5]**
		(c) Consider use of a flow diagram **[N/A]**
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders **[8-9]**
		(b) Indicate number of participants with missing data for each variable of interest **[8]**
Outcome data	15*	Report numbers of outcome events or summary measures **[9]**
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included **[10]**
		(*b*) Report category boundaries when continuous variables were categorized **[7,11]**

		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period **[N/A]**
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses **[11]**
Discussion		
Key results	18	Summarise key results with reference to study objectives **[11-12]**
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias **[13-14]**
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence**[13]**
Generalisability	21	Discuss the generalisability (external validity) of the study results **[13]**
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based **[14]**

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.