

Prevalence of microalbuminuria in the general population of Seychelles and strong association with diabetes and hypertension independent of renal markers

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Objective Few studies have examined microalbuminuria (MAU) in non-western populations. We assessed the prevalence of MAU in the general population of a middle-income country in the African region and relationships between MAU and selected cardiovascular risk factors.

Methods An examination survey was conducted in a sample representative of the entire population aged 25–64 years in the Seychelles. MAU adjusted for urine creatinine concentration was measured on the second morning urine using a semiquantitative point-of-care analyzer.

Results A total of 1255 persons attended the survey (participation rate of 80.2%). The age-adjusted prevalence of MAU was 11.4%. At age 25–64 years, the prevalence of MAU was 5% in persons without diabetes and hypertension, 20% in persons with either condition and 41% in persons with both conditions. The overall prevalence of stages 3–4 chronic kidney disease was low at 3.2%. In multivariate analysis, MAU was associated with age [odds ratio (OR) 1.24 for a 10-year increase; 95% confidence interval (CI): 1.02–1.52], hypertension stage I (2.0; 1.1–3.8) and stage II (4.5; 2.3–8.6), obesity (1.7; 1.0–2.8) and diabetes (3.0; 1.9–4.9). These associations were virtually unchanged upon further adjustment for markers of renal function such as serum creatinine, serum cystatin C and calculated renal function.

Introduction

Microalbuminuria (MAU) is defined as an increased urine albumin excretion (30–300 mg per 24 h) that is undetectable by standard protein dipstick testing [1]. MAU has been recognized as an early sign of renal damage and a predictor of end-stage renal disease in diabetic patients [2,3]. In addition, MAU is recognized as a predictor of cardiovascular morbidity and mortality, even in the absence of diabetes or overt impaired kidney function [4–7]. These relationships of MAU with both renal function and cardiovascular risk suggest that screening for MAU is a useful additional test for identifying persons at risk for developing renal and cardiovascular complications [8].

A limitation in defining a universal role of MAU as a tool for surveillance or screening is the paucity of both pre-

Conclusion The prevalence of MAU was high in this population, and MAU was strongly associated with several cardiovascular risk factors independently of renal function markers. These findings suggest that MAU could be a useful marker of cardiovascular risk in this population and help identify persons in need of a specific cardiovascular risk management. *J Hypertens* 26:871–877 © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Abbreviations: MAU, microalbuminuria; ACR, albumin/creatinine ratio; 4v-MDRD, Modification of Diet in Renal Disease; CKD, stages of chronic kidney disease; BMI, body mass index; BP, blood pressure; FBG, fasting blood glucose; HDL, high-density lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LDL, low-density lipoprotein; 2hG, glucose 2 h after 75 g glucose meal

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valence and outcome data in several populations. In particular, the prevalence of MAU is largely unknown in non-western populations [9] and we are not aware of any population-based survey in the African region.

The gold standard for MAU measurement is based on 24-h urine collection [1]. Alternatively, MAU can be assessed using nontimed random spot urine sampling [10]. Spot sample-based tests are generally adjusted to creatinuria to take into account the variation in urinary flow rate and concentration and the test is considered positive for the albumin/creatinine ratio (ACR) of 30–300 mg albumin/g creatinine, corresponding to 3.4–33.9 mg albumin/mmol creatinine [11,12]. ACR can be measured either quantitatively or semiquantitatively. Semiquantitative ACR, which can be done using a point-of-care analyzer and fairly inexpensive reagents,

correlates well with albuminuria measured using (quantitative) reference laboratory methods and some of these tests (like the one used in this study) have been recognized as valid screening method [1,11,13].

The aim of this study was to estimate the prevalence of MAU using semiquantitative spot urine sampling in the general population of the Seychelles, a rapidly developing country in the African region, and to investigate the relationship between MAU and selected cardiovascular risk factors in this population.

Methods

The Republic of Seychelles is a group of islands in the Indian Ocean situated 2000 km east of Kenya. Although intermarriage has blurred racial differences in many inhabitants, it can be considered that approximately two-thirds of the population are of predominantly African descent, 15% are of white, Indian or Chinese descent and a fifth are mixed between these various groups. The national gross domestic product per capita, in real terms, increased from US\$2927 in 1980 to US\$5239 in 2004, reflecting booming tourism and industrial fishing industries. Increased levels of cardiovascular risk factors, particularly overweight, hypertension and diabetes, have been documented in the adult population in 1989 and 2004 [14,15].

In 2004, a population-based survey of cardiovascular risk factors was conducted (Seychelles Heart Study III). The methods of the survey have been reported previously [15]. Briefly, a random sex-stratified and age-stratified sample of all inhabitants aged 25–64 years was drawn using computerized data of a national population census carried out in 2002 and thereafter regularly updated by civil status authorities. Eligible persons were invited by letter to join one of the study centers. The survey was approved by the Ministry of Health. Persons were free to participate and gave written informed consent.

Weight and height were measured and body mass index (BMI) was calculated. Blood pressure (BP) was measured several times in persons seated for at least 30 min, using a cuff adjusted to the arm circumference. We used the average of the second and third measurement, obtained with a mercury sphygmomanometer. BP categories followed usual recommendations [16].

Venous blood was drawn in the morning after an overnight fast. All samples were centrifuged within 2 h of blood collection and plasma was immediately frozen to -20°C . Blood sugar was measured using a Cholestec point-of-care analyzer. If the value was at least 5.6 mmol/l, an additional capillary measurement – adjusted for plasma values – was carried out (Ascencia Elite glucometer; Bayer, Leverkusen, Germany) and the average of the two readings was considered. An oral glucose tolerance test

was performed if the fasting blood glucose concentration was at least 5.6 mmol/l and less than 7 mmol/l and with no reported history of diabetes [17]. Other analyses were performed in the Laboratory of the Kantonspital, St Gallen (Switzerland) and included creatinine, cystatin C, high-density lipoprotein cholesterol (HDL-c) and triglycerides. Low-density lipoprotein cholesterol (LDL-c) was calculated with the Friedewald formula. The Modification of Diet in Renal Disease-formula (4v-MDRD) was used to estimate the creatinine clearance [18]. Stages of chronic kidney disease (CKD) were classified along the K/DOQI guidelines [19].

Microalbuminuria was measured with a Clinitek Status analyzer (Bayer) on a spot of the second morning urine (0800–1100 h) after an overnight fast. We used the second morning urine instead of the first morning urine for practical reasons as participants had to be examined in a few study centers and travel accordingly (most often by bus, travel duration of <1 h in most cases). This analyzer uses a sulphonephthalein dye binding to measure albumin and the peroxidase-like activity of copper creatinine complexes to measure creatinine. The color yields of the separate reaction pads are monitored by a reflectance photometer and compared with a preprogrammed calibration algorithm [20]. Thus, it provides four categories of albumin concentration (10, 30, 80 and 150 mg/l) and five categories of creatinine concentration (0.9, 4.4, 8.8, 17.7 and 26.5 mmol/l), as well as three calculated categories of ACR: normal albuminuria (< 3.4 mg albumin/mmol creatinine), microalbuminuria (3.4–33.9 mg albumin/mmol creatinine) and macroalbuminuria (> 33.9 mg albumin/mmol creatinine).

These categories are based on an in-built preprogrammed calculation by the device that cannot be modified and on the – preprogrammed – classic definition of MAU (3.4–33.9 mg albumin/mmol creatinine).

The distribution of cardiovascular risk factors (mean values and prevalence) was standardized for age using the new World Health Organization standard population [21]. Differences in age-standardized estimates were tested using Student's *t*-test for continuous variables and χ^2 -test for categorical variables. We examined the univariate and multivariate relationships between microalbuminuria and other cardiovascular risk factors and other markers of renal function using logistic regression analysis, appropriately weighted for the stratified study design. All *P*-values were two-sided and values less than 0.05 were considered significant. Analyses were performed using SPSS software version 14.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Of the 1563 eligible persons, 1255 participated in the survey, a participation rate of 80.2%. This study refers to

Table 1 Prevalence (%) of microalbuminuria and macroalbuminuria by age and sex

	Age				
	25–34 years	35–44 years	45–54 years	55–64 years	25–64 ^a years
Men					
<i>N</i>	124	134	158	143	559
Normal	96.8 (1.6)	91.0 (2.5)	84.8 (2.9)	74.9 (3.6)	88.7 (1.2)
Microalbuminuria	3.2 (1.6)	9.0 (2.5)	14.6 (2.8)	23.1 (3.5)	10.8 (1.3)
Macroalbuminuria	0	0	0.6 (0.6)	2.1 (1.2)	0.5 (0.2)
Women					
<i>N</i>	140	164	176	179	659
Normal	95.7 (2.5)	90.9 (2.7)	81.9 (3.0)	70.7 (3.4)	87.0 (1.4)
Microalbuminuria	4.3 (2.4)	8.5 (2.6)	17.5 (2.9)	23.8 (3.2)	12.1 (1.4)
Macroalbuminuria	0	0.6 (0.8)	0	4.4 (1.5)	0.9 (0.4)
Total					
<i>N</i>	264	298	334	322	1218
Normal	96.2 (1.5)	90.9 (1.9)	83.5 (2.1)	73.0 (2.5)	87.9 (1.0)
Microalbuminuria	3.8 (1.5)	8.7 (1.8)	16.2 (2.0)	23.6 (2.3)	11.4 (0.9)
Macroalbuminuria	0	0.4 (0.5)	0.3 (0.4)	3.4 (1.0)	0.7 (0.2)

Standard error is given within parentheses. ^aStandardized for age.

1218 participants after exclusion of 25 persons reporting menstruations or acute urinary tract infections and 12 persons with incomplete data. The prevalence of CKD stages 3–5 was low in participants in this survey [19]. No participant had CKD stage 5; CKD stage 4 was found in 0.3% of participants aged 55–64 years, CKD stage 3 was found in 7.1% of participants aged 55–64 years; overall, 3.2% of participants had CKD stages 3–4.

The prevalence of MAU according to sex and age is shown in Table 1. Overall, the prevalence of MAU increased from 3.8% at age 25–34 years to 23.6% at age 55–64 years. The prevalence of MAU was slightly higher in women than in men, irrespective of age. Examined separately, albuminuria increased over age categories whereas creatinuria did not. A total of 87.3% of subjects had urine creatinine values of 8.8 mmol/l or higher. This suggests that most subjects had rather concentrated urine.

Table 2 shows the prevalence of MAU by categories of sex, age, high blood pressure (HBP) and diabetes, stratified by age and sex. Estimates for age 25–64 years are

standardized for age. The patterns of prevalence of MAU across categories of HBP and diabetes were largely similar in men and in women. Overall (men and women aged 25–65 years), the prevalence of MAU increased largely across categories of BP (respectively 7 vs. 24% in persons with less or more than 140/90 mmHg, $P < 0.01$) and categories of blood glucose (respectively 8 vs. 36% in persons with or without diabetes, $P < 0.01$). Note that prevalence of MAU among persons with ‘hypertension’ (first four rows in Table 2) is in contrast to persons ‘without hypertension’; hence, these persons may or may not also have diabetes. The same remark applies for categories of diabetes (rows 5–7 in Table 2) and these persons may or may not also have hypertension. The prevalence of MAU increased gradually across categories of normal BP, hypertension stage 1 and hypertension stage 2 (respectively 7, 18 and 34%; $P < 0.01$ for all differences). Similarly, the prevalence of MAU increased gradually across categories of normal blood glucose, impaired glucose tolerance and diabetes (respectively 8, 17 and 36%; $P < 0.01$ for all differences). The prevalence of MAU was low among persons of all ages without diabetes or HBP (5%), as compared with 20% in persons

Table 2 Prevalence (in percentage) of microalbuminuria in persons with hypertension, diabetes or both conditions

	Men			Women			Total		
	25–44 years	45–64 years	25–64 years	25–44 years	45–64 years	25–64 years	25–44 years	45–64 years	25–64 years
No hypertension (<140/90 mmHg)	2.8 (1.2)	8.5 (2.5)	4.6 (1.2)	6.3 (1.5)	15.5 (2.6)	8.6 (1.3)	4.8 (1.0)	12.8 (1.8)	6.8 (0.9)
Hypertension stage I (140–159/90–99 mmHg)	13.5 (4.8)	20.8 (4.1)	16.5 (3.0)	12.9 (6.1)	26.6 (4.6)	21.0 (3.7)	13.3 (3.7)	23.6 (3.0)	18.2 (2.3)
Hypertension stage II ($\geq 160/90$ mmHg)	17.6 (9.5)	39.4 (5.8)	32.4 (5.0)	11.1 (11.1)	42.6 (6.4)	36.3 (5.8)	15.4 (7.2)	40.9 (4.3)	33.9 (3.8)
All hypertensives ($\geq 140/90$ mmHg)	14.3 (4.2)	28.5 (3.5)	22.0 (2.7)	12.5 (5.3)	32.9 (3.8)	26.3 (3.2)	13.6 (3.3)	30.6 (2.6)	23.7 (2.0)
Neither diabetes nor IGT	4.5 (1.4)	12.0 (2.5)	6.7 (1.3)	5.6 (1.4)	15.7 (2.6)	8.6 (1.3)	5.1 (1.0)	14.0 (1.8)	7.6 (0.9)
IGT	5.0 (5.0)	19.7 (5.1)	14.3 (3.9)	4.8 (4.8)	27.4 (5.7)	19.3 (4.4)	4.9 (3.4)	23.6 (3.8)	16.6 (2.9)
Diabetes	33.3 (12.6)	41.5 (6.2)	38.2 (5.5)	31.3 (12.0)	37.1 (5.1)	34.1 (4.6)	32.3 (8.5)	39.0 (3.9)	36.1 (3.5)
Neither hypertension nor diabetes	2.2 (1.1)	5.3 (2.1)	3.0 (1.0)	5.1 (1.4)	12.6 (2.6)	6.8 (1.2)	3.9 (0.9)	9.6 (1.8)	5.0 (0.8)
Hypertension or diabetes	13.0 (4.1)	23.0 (3.6)	18.4 (2.7)	13.6 (5.2)	27.0 (3.7)	23.0 (3.0)	13.3 (3.2)	25.1 (2.6)	20.3 (2.0)
Hypertension and diabetes	36.6 (18.2)	43.1 (7.1)	41.6 (6.6)	31.6 (20.8)	42.8 (7.2)	40.9 (6.8)	34.7 (13.2)	43.0 (5.1)	41.3 (4.7)

Standard error is given within parentheses. Prevalence for categories 25–64 years is standardized for age. Participants with macroalbuminuria were excluded from this analysis. IGT, impaired glucose tolerance.

Table 3 Relationships between microalbuminuria and selected risk factors

Variable	Criterion	Prevalence (%) ^a	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P	
Age category	25–34	22.2 (1.2)	1		1		
	35–44	25.1 (1.2)	2.44 (1.15–5.15)	< 0.005	1.67 (0.77–3.63)	NS	
	45–54	27.4 (1.3)	4.92 (2.45–9.86)	< 0.005	2.34 (1.12–4.91)	0.024	
	55–64	25.3 (1.3)	8.21 (4.15–16.3)	< 0.005	2.99 (1.41–6.35)	< 0.005	
Sex	Women vs. men	49.1 (15)–50.9(15)	1.13 (0.82–1.58)	NS	1.25 (0.82–1.91)	NS	
Smoking	Yes vs. no	17.7 (1.8)–82.3(1.1)	1.01 (0.65–1.57)	NS	1.44 (0.84–2.31)	NS	
Body mass index (kg/m ²)	Normal	< 25	40.1 (1.5)	1	1		
	Overweight	25–29	35.2 (1.4)	1.65 (1.06–2.55)	0.026	1.13 (0.69–1.84)	NS
	Obese	≥ 30	24.7 (1.3)	3.11 (2.03–4.75)	< 0.005	1.70 (1.01–2.84)	0.044
Blood pressure (mmHg)	Normal	< 120/80	30.0 (1.4)	1	1		
	Prehypertension	120–39/80–89	38.1 (1.5)	1.82 (1.03–3.22)	0.039	1.22 (0.67–2.23)	NS
	Stage I	140–59/90–99	20.9 (1.2)	4.11 (2.34–7.21)	< 0.005	2.02 (1.08–3.78)	0.029
	Stage II	>160/100	11.0 (0.9)	8.96 (5.01–16.0)	< 0.005	4.47 (2.33–8.57)	< 0.005
Glucose metabolism (mmol/l)	Normal	< 5.6	62.9 (1.4)	1	1		
	IFG and no IGT	5.6–6.9	13.9 (1.0)	1.46 (0.84–2.54)	NS	1.03 (0.57–1.84)	NS
	IGT	2hG: 7.8–11.1	11.8 (0.9)	2.71 (1.68–4.38)	< 0.005	1.50 (0.89–2.53)	NS
	Diabetes	FBG ≥ 7 or 2hG ≥ 11.1	11.4 (0.9)	6.17 (4.08–9.35)	< 0.005	3.04 (1.89–4.89)	< 0.005
LDL cholesterol (mmol/l)		3.6 (1.2)	1.26 (1.12–1.43)	< 0.005	1.10 (0.96–1.27)	NS	
HDL cholesterol (mmol/l)		1.4 (0.5)	0.76 (0.53–1.08)	NS	1.01 (0.68–1.51)	NS	

Participants with macroalbuminuria were excluded from this analysis. Prevalence is standardized for age. CI, confidence interval; FBG, fasting blood glucose; HDL, high-density lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LDL, low-density lipoprotein; OR, odds ratio; 2hG, glucose 2 h after 75 g glucose meal. ^aStandard error is given within parentheses.

with either hypertension or diabetes and 41% in persons with both hypertension and diabetes ($P < 0.001$ for all differences).

Table 3 shows the univariate and multivariate relationships between MAU and selected cardiovascular risk factors. Participants with macroalbuminuria are not included in these analyses. In univariate analysis, MAU was strongly associated with age, overweight/obesity ($BMI \geq 25 \text{ kg/m}^2$), HBP categories, glucose metabolism categories and LDL-c. Multivariate analysis showed that age, obesity ($BMI \geq 30 \text{ kg/m}^2$), hypertension and diabetes remained associated with MAU. Analyses conducted separately in men and in women showed largely similar patterns of associations, except for an association with obesity in women [odds ratio (OR) 3.0; 95% confidence interval (CI) 1.4–6.4] but not in men (0.69; 95% CI: 0.29–1.63) and a trend toward a stronger association with hypertension and diabetes in men than in women.

Multivariate OR shown in Table 3 relating diabetes and hypertension to MAU remained virtually identical upon further adjustment for renal function markers (creatinine, cystatin C and 4v-MDRD) alone or in combination (data not shown). For example, the OR for diabetes was 3.02 (2.83–3.23) without adjustment for renal markers and 2.91 (2.71–3.12) with adjustment for creatinine, cystatin C and 4v-MDRD. This indicates that the relationships between MAU and hypertension and diabetes are largely independent of renal function markers.

Discussion

Taken together, the results of this analysis show a high prevalence of microalbuminuria in the general adult

population of Seychelles, a strong association between microalbuminuria and hypertension and diabetes and that these associations are independent of renal function markers.

We are not aware of any previous large-scale, population-based estimate of the prevalence of MAU in the African region. The prevalence of MAU at age 25–64 years (11.4%) was high in the population of Seychelles as compared with the population-based data of western countries. The prevalence of MAU in predominantly white populations ranged between 6 and 11.6% (Table 4 [22–28]) and was approximately 7% in African Americans aged more than 6 years [29,30]. Compared with white individuals, African individuals tend to have higher muscle mass, hence higher urine creatinine excretion and lower rates of creatinine-adjusted MAU [31]. This systematic difference would tend to underestimate the prevalence of MAU in Seychelles as compared with the studies in white individuals [31].

Several factors underlie the high prevalence of MAU in our study. First, the prevalence of hypertension (e.g. 32% with BP $\geq 140/90$ mmHg at age 25–64 years) and diabetes (11% at age 25–64 years) is high in the Seychelles by International Standards [15]. Approximately, one-third (36.1%) of persons with diabetes had MAU and this percentage increased further (to 41.6%) in the presence of associated hypertension, underlining the additional effect of these conditions on MAU. Second, the prevalence of obesity is also high in Seychelles (e.g. 25% at age 25–64 years). Excess body weight has been reported to be associated with MAU and albuminuria independently of other risk factors such as hypertension and diabetes

Table 4 Review of large studies that have reported the prevalence of microalbuminuria in the general population

Study	Country, year of study	Participants (n)	Population			Prevalence of MAU (%)
			Age (mean) (years)	Area, sampling	Diabetics (%)	
Association between albuminuria and proteinuria in the general population (Aus Diab Study) [27]	Australia, 1999–2000	11 247	> 25 (49)	Total population, random	1.8	6
European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) [24]	United Kingdom, 1993–97	23 630	40–79 (63)	Urban, random	2.2	11.6
Nord-Trøndelag Health Study (HUNT) [23]	Norway, 1995–97	2113	20–80 (49)	Total population, random	0 (diabetics excluded)	1.5–23.8
Hillege <i>et al.</i> [28]	Zimbabwe, 1999	370	> 25	Urban – only women, random	Unspecified	8
Jacobs <i>et al.</i> [25]	Singapore, 1997	19 848	65–73 (70.6)	Urban, random	14.3	8.5
NHANES III [22]	United States, 1988–94	22 244	6–80	Total population, random	5.9	7.9
Prevention of Renal and Vascular End Stage Disease (PREVEND) [26]	The Netherlands, 1997–98	40 619	28–75 (49.5)	Urban, random	2.6	7.2
Seychelles Heart Study III	Seychelles, 2004	1 255	25–64 (45)	Total population, random sample	11.0	11.4

MAU, microalbuminuria.

[22]. The high prevalence of MAU in the population of Seychelles illustrates the changing epidemiological situation related to the rapid emergence of noncommunicable diseases in countries in health transition and the subsequent new challenges for healthcare systems [32].

The prevalence of MAU was slightly higher in women than in men in our study, whereas the reverse was found in several other populations [33–35]. Increased prevalence of MAU in women than in men might be related to lower muscle mass – hence creatininuria – in women. Therefore, some authors [23–25] have suggested the use of sex-related cut-off values to define MAU (2.5–30 mg/mmol for men and 3.5–30 mg/mmol for women). There is however, so far, no definite consensus and some current recommendations advise for sex-specific cut-offs [24,25,36] whereas others do not [26,27]. Furthermore, the semiquantitative method used in this study has not been developed to provide sex-specific results. Using a sex-specific threshold, however, might result in a MAU prevalence moderately higher in men and lower in women as compared with the current results, but the overall MAU prevalence might not be altered substantially. Such sex-specific criteria might have a particular impact on the prevalence of MAU in the youngest age category in which muscle mass – hence urinary creatinine excretion – is high. Although the increased prevalence of MAU in women than in men in our study may relate, in part, to the chosen cut offs, this difference is also consistent with a markedly increased prevalence of overweight in women than in men in Seychelles [15], as obesity has been found to be an independent risk factor of MAU.

The strong associations between MAU and both hypertension and diabetes in the Seychelles are consistent with findings in other populations [28,34,35,37,38]. The mechanisms underlying these relationships are still debated.

There is increasing evidence for a causal pathway linking diabetes, hypertension and the metabolic syndrome to systemic (including glomerular) endothelial dysfunction [39], increased vessel wall permeability and leakage of lipoproteins and albumin (including MAU) and, finally, accelerated atherosclerosis [40]. These mechanisms might also explain the higher cardiovascular mortality found in persons with MAU [5].

The relationships between MAU and hypertension and diabetes remained largely unchanged upon adjustment for markers of renal function such as creatinine, 4v-MDRD and cystatin C in our study. This finding is consistent with the hypothesis that MAU is the consequence of systemic dysfunction (e.g. endothelial dysfunction) rather than the sole consequence of renal impairment. This is also consistent with the evidence that the presence of MAU independently increases cardiovascular risk in persons with diabetes and/or hypertension [7,33,34]. In the Framingham study [6], MAU was shown to independently increase the cardiovascular risk by three-fold. The cross-sectional design of our study, however, precludes firm conclusions on causality.

The use of a semiquantitative method for MAU screening in our study is another limitation. This can be a source of some misclassification but we do not expect a systematic bias in the overall prevalence estimate. Other studies [1,13,15,41] have used semiquantitative devices as they correlate well with quantitative methods, as shown, for example, by a sensitivity of 75–85% and a specificity of 85–94% when compared with the latter.

Our study raises the question of the potential usefulness of MAU screening for identifying persons at increased risk of cardiovascular and/or renal complications in populations experiencing epidemiological transition.

MAU screening is attractive and possibly cost-effective [42] as it is technically easy to perform (e.g. spot urine, inexpensive reagents and no need for the intervention of a specialist) and it gives information on both cardiovascular and renal risk [43].

Nevertheless, several issues deserve attention. First, it is not established whether persons with isolated MAU should receive treatment [e.g. angiotensin-converting enzyme (ACE) inhibitor] although some recent studies [8,44] (in western countries) showed a reduction in cardiovascular events and urinary albumin excretion in persons treated with an ACE inhibitor as primary prevention. Second, screening strategies need more clarification: which individuals should be screened (e.g. in terms of associated risk factors or absolute risk stratification) and how MAU should be assessed (e.g. albuminuria vs. ACR, modalities for urine collection, need for confirmatory test if a first test is positive). Third, more data are needed to show that MAU screening would improve treatment as compared with therapeutic decisions based on medical information other than MAU (e.g. medical history, physical examination, risk factors and so on). On that note, MAU could also constitute a tool for health education and studies could examine whether patients aware of MAU would be, for example, more motivated to adhere to treatment (e.g. lifestyle changes, medication for hypertension or diabetes). Fourth, more studies are needed to expand our knowledge on the prevalence of MAU in different populations and the relationship between MAU and cardiovascular and renal outcomes in these populations. In a context of low resource settings, and given that MAU determination is noninvasive and relatively inexpensive (e.g. US\$2–3 per test), MAU could serve as a simple means for assessing an individual's cardiovascular risk, and perhaps particularly when risk stratification cannot rely on more invasive tests, including blood lipids.

In conclusion, our study provides the first estimate of the prevalence of MAU in an African population in health transition. By showing strong associations between MAU and cardiovascular risk factors, our findings suggest that MAU could be a useful marker of cardiovascular risk to help identify patients in need of intensified cardiovascular risk management. Further prevalence and outcome studies in different populations are needed to further guide consensus on the value of MAU as a screening tool for renal and/or cardiovascular diseases.

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References

- Rowe DJ, Dawney A, Watts GF. Microalbuminuria in diabetic subjects. *Ann Clin Biochem* 1990; **27**:297–312.
- Mogensen CE. Microalbuminuria as predictor of clinical diabetic nephropathy. *Kidney Int* 1987; **31**:673–689.
- Viberti GC, Hill RD, Jarrett RJ, Argyropoulos A, Mahmud U, Keen H. Microalbuminuria as a predictor of clinical nephropathy in insulin-dependent diabetes mellitus. *Lancet* 1982; **26**:1430–1432.
- Yudkin JS, Forrester RD, Jackson CA. Microalbuminuria as a predictor of vascular disease in nondiabetic subjects. Islington diabetes survey. *Lancet* 1988; **2**:530–533.
- Hillege HL, Fidler V, Diercks GF, van Gilst WH, de Zeeuw D, van Veldhuisen DJ, et al. Urinary albumin excretion predicts cardiovascular and noncardiovascular mortality in general population. *Circulation* 2002; **106**:1777–1782.
- Arnlov J, Evans JC, Meigs JB, Wang TJ, Fox CS, Levy D, et al. Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: the Framingham heart study. *Circulation* 2005; **112**:969–975.
- Gerstein HC, Mann JF, Yi Q, Zinaman B, Dinneen SF, Hoogwerf B, et al. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 2001; **286**:421–426.
- de Jong PE, Hillege HL, Joan Pinto-Sietsma, de Zeeuw D. Screening for microalbuminuria in the general population: a tool to detect subjects at increased risk for progressive renal failure in an early phase? *Nephrol Dial Transplant* 2003; **18**:10–13.
- Perico N, Plata R, Anabaya A, Codreanu I, Schieppati A, Ruggenenti P, Remuzzi G. Strategies for national healthcare systems in emerging countries: the case of screening and prevention of renal disease progression in Bolivia. *Kidney Int* 2005; **97** (Suppl):87–94.
- American Diabetes Association. Diabetic nephropathy. *Diabetes Care* 2001; **25** (Suppl 1):S85–S89.
- Croal BL, Mutch WJ, Clark BM, Dickie A, Church J, Noble D, et al. The clinical application of a urine albumin:creatinine ratio point-of-care device. *Clin Chim Acta* 2001; **307**:15–21.
- Marshall SM. Screening for MAU: which measurement? *Diabet Med* 1991; **8**:706–711.
- American Diabetes Association (ADA). Diabetic nephropathy. *Diabetes Care* 1997; **20**:S24–S27.
- Bovet P, Shamlaye C, Kitua A, Riesen WF, Paccaud F, Darioli R. High prevalence of cardiovascular risk factors in the Seychelles (Indian Ocean). *Arterioscler Thromb* 1991; **11**:1730–1736.
- Bovet P, Shamlaye C, Gabriel A, Riesen W, Paccaud F. Prevalence of cardiovascular risk factors in a middle income country and estimated cost of a treatment strategy. *BMC Public Health* 2006; **6**:9.
- Chobanian AV, Bakris GL, Black HR, Cushman WL, Green LA, Izzo JL Jr, et al. The seventh report of the joint national committee on prevention, detection, evaluation and treatment of high blood pressure. *JAMA* 2003; **19**:2560–2572.
- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1. diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 1998; **15**:539–553.
- Traynor J, Mactier R, Geddes CC, Fox JG. How to measure renal function in clinical practice. *BMJ* 2006; **333**:733–737.
- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Am J Kidney Dis* 2002; **39** (Suppl 1):S21–S26.
- Parsons M, Newman DJ, Pugia M, Pugia M, Newall RG, Price CP. Performance of a reagent strip device for quantification of the urine albumin: creatinine ratio in a point of care setting. *Clin Nephrol* 1999; **51**:220–227.
- Ahmad OB, Boschi-Pinto C, Lopez AD, Murray CJL, Lozano R, Inoue M. Age standardization of rates: a new WHO standard. In: *Global program on evidence for health policy*; Paper Series No 31. Geneva: World Health Organization.
- Rutkowski P, Klassen A, Sebekova K, Bahner U, Heidland A. Renal disease in obesity: the need for greater attention. *J Ren Nutr* 2006; **16**:216–223.
- Mattix HJ, Hsu CY, Shaykevich S, Curhan G. Use of albumin/creatinine ratio to detect microalbuminuria: implications of sex and race. *J Am Soc Nephrol* 2002; **13**:1034–1039.
- Karalliedde J, Viberti G. Microalbuminuria and cardiovascular risk. *Am J Hypertens* 2004; **17**:986–993.
- Jacobs DR, Murtaugh MA, Steffes M, Yu X, Roseman J, Goetz FC. Gender- and race-specific determination of albumin-to-creatinine ratio in single, untimed urine specimens: the Coronary Artery Risk Development in Young Adults Study. *Am J Epidemiol* 2002; **155**:1114–1119.

- 26 American Diabetes Association. Standards of medical care in diabetes-2007. *Diabetes Care* 2007; **30**:S42–S47.
- 27 Levey AS, Coresh J, Balk E, Kausz A, Levin A, Steffes MW, *et al.* National Kidney Foundation Practice Guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med* 2003; **139**:137–147.
- 28 Hillege HL, Janssen WM, Bak AA, Diercks GF, Grobbee DE, Crijs HJ, *et al.* Microalbuminuria is common, also in nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular mortality. *J Intern Med* 2001; **249**:519–526.
- 29 Jones CA, Francis ME, Eberhardt MS, Chavers B, Coresh J, Engलगau M, *et al.* Microalbuminuria in the US population: third national health and nutrition examination survey. *Am J Kidney Dis* 2002; **39**:445–459.
- 30 Tillin T, Forouhi N, McKeigue P, Chaturvedi N. Microalbuminuria and coronary heart disease risk in an ethnically diverse UK population: a prospective cohort study. *J Am Soc Nephrol* 2005; **16**:3702–3710.
- 31 James GD, Sealey JE, Alderman M, Ljungman S, Mueller FB, Pecker MS, Laragh JH. A longitudinal study of urine creatinine and creatinine clearance in normal subjects. Race, sex and age differences. *Am J Hypertens* 1988; **1**:124–131.
- 32 Lawoyin TO, Asuzu MC, Kaufman J, Rotimi C, Owoaje E, Johnson L, Cooper R. Prevalence of cardiovascular risk factors in an African, urban inner city community. *West Afr J Med* 2002; **21**:208–211.
- 33 Romundstad S, Holmen J, Hallan H, Kvenild K, Krüger O, Midthjell K. Microalbuminuria, cardiovascular disease and risk factors in a nondiabetic/nonhypertensive population. The Nord-Trøndelag Health Study (HUNT, 1995-97), Norway. *J Intern Med* 2002; **252**:164–172.
- 34 Yuyun M, Khaw KT, Luben R, Welch A, Bingham S, Day NE, Wareham NJ. Microalbuminuria and stroke in a British population: the European prospective investigation into cancer in Norfolk (EPIC-Norfolk) population study. *J Intern Med* 2004; **255**:247–256.
- 35 Joshi VD, Nandkumar M, Lim J. Prevalence and risk factors of undetected proteinuria in an elderly South-East Asian population. *Nephrology* 2006; **11**:347–354.
- 36 Warram JH, Gearin G, Laffel L, Krolewski AS. Effect of duration of type 1 diabetes on the prevalence of stages of diabetic nephropathy defined by urinary albumin/creatinine ratio. *J Am Soc Nephrol* 1996; **7**:930–937.
- 37 Atkins RC, Polkinghorne KR, Briganti EM, Shaw E, Zimmet PZ, Chadban SJ. Prevalence of albuminuria in Australia: the AusDiab kidney study. *Kidney Int* 2004; **92 (Suppl)**:S22–S24.
- 38 Hwang KK, Scott LJ, Chifamba J, Mufunda J, Spielman WS, Sparks HV. Microalbuminuria in urban Zimbabwean women. *J Hum Hypertens* 2000; **14**:587–593.
- 39 Chen J, Muntner P, Hamm LL, Jones DW, Batuman V, Fonseca V, *et al.* The metabolic syndrome and chronic kidney disease in US adults. *Ann Intern Med* 2004; **140**:167–174.
- 40 Deckert T, Feldt-Rasmussen B, Borch-Johnsen K, Jensen T, Kofoed-Enevoldsen A. Albuminuria reflects widespread vascular damage. The Steno hypothesis. *Diabetologia* 1989; **32**:219–226.
- 41 Nathan DM, Rosenbaum C, Protasowicki VD. Single-void urine samples can be used to estimate quantitative microalbuminuria. *Diabetes Care* 1987; **10**:414–418.
- 42 Athobari J, Asselbergs FW, Boersma C, de Vries R, Hillege HL, van Gilst Wh, *et al.* Cost-effectiveness of screening for albuminuria with subsequent foscipril treatment to prevent cardiovascular events: a pharmacoeconomic analysis linked to the renal and vascular endstage disease (PREVEND) study and the prevention of renal and vascular endstage disease intervention trial (PREVEND IT). *Clin Ther* 2006; **28**:432–444.
- 43 Verhave JC, Gansevoort RT, Hillege HL, Bakker SJ, de Zeeuw D, de Jong PE. An elevated urinary albumin excretion predicts de novo development of renal function impairment in the general population. *Kidney Int* 2004; **66 (Suppl 92)**:S1–S4.
- 44 Asselbergs FW, Diercks GF, Hillege HL, van Boven AJ, Janssen WM, Voors AA, *et al.* Effects of foscipril and pravastatin on cardiovascular events in subjects with microalbuminuria. *Circulation* 2004; **110**:2809–2816.