

Screening for Proteinuria and Chronic Kidney Disease Risk Factors in Kinshasa: A World Kidney Day 2007 Study

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Key Words

Chronic kidney disease · Diabetes mellitus · Developing countries · Early detection

Abstract

Background: Although screening programs for chronic kidney disease (CKD) may be of great value, these programs are not yet implemented in the Democratic Republic of Congo. This study focused on proteinuria and examined its prevalence in terms of the number needed to screen for the different risk factors of CKD. Such knowledge would guide the utility of population screening to prevent end-stage renal disease. **Methods:** A cross-sectional survey was conducted in Kinshasa on the Second World Kidney Day. A sample of 3,018 subjects was interviewed and the following measurements were performed: blood pressure, body mass index, glycemia and urine protein. Logistic regression analysis was used to identify determinants of proteinuria. **Results:** The prevalence of proteinuria was 17.1% (95% CI 15.8–18.6). Other CKD risk factors identified were: hypertension, diabetes mellitus, obesity and metabolic syndrome. To identify 1 case of proteinuria, one would need to screen 4 persons with dia-

betes, 5 persons with hypertension, 4 subjects having metabolic syndrome, 5 persons aged ≥ 72 years and 9 persons without any of the conditions mentioned above. Age, overweight and diabetes were the strongest factors associated with proteinuria. **Conclusions:** This study indicates that proteinuria and traditional risk factors for CKD are very prevalent in Kinshasa. Realistic policies to stem these conditions should be a public health priority.

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Introduction

Chronic kidney disease (CKD) is a worldwide public health problem [1]. To cope with this epidemic, community-based prevention is a necessary strategy and must be based on education, early detection and effective management of CKD and its associated risk factors [2]. Indeed, screening programs are integral components of existing CKD prevention programs. These strategies have already shown promising results in both developed and developing countries [3–5].

However, the effectiveness of the strategy will depend on local infrastructure, finances and organization [6]. Unfortunately, many countries in sub-Saharan Africa including the Democratic Republic of Congo (DRC) have low capacity and resources to accomplish this. In some of them, the health expenditure per capita does not exceed USD 10 per year [7], and this is clearly insufficient to address the challenges posed by the double burden of infectious and noncommunicable diseases (NCD), including CKD.

In addition, the paucity of symptoms and signs in early CKD leads to delays in its recognition [8]. Thus, community strategies to reduce incidence of end-stage renal disease (ESRD) may need to integrate methods of screening and early intervention adapted to the ability of the local team and facilities. Proteinuria is a well-recognized predictor of ESRD and cardiovascular as well as all-cause mortality rates [9, 10]. Furthermore, several studies suggest that low grades of proteinuria or microalbuminuria might be associated with early CKD even in a nondiabetic population [10, 11]. Moreover, screening for proteinuria often alerts the physician to the presence of CKD before changes in the glomerular filtration rate (GFR) become apparent and even precede the diagnosis of hypertension or diabetes [12]. Therefore, determination of risk factors for the development of proteinuria might facilitate focused preventive and therapeutic tools to delay the progression of CKD.

Previous studies have suggested that markers for cardiovascular disease are also risk factors for renal disease and proteinuria [13, 14]. However, those studies were focused primarily on Caucasian, African-American and Asian populations [14, 15]. Also, because Black Africans are at increasing risk of developing ESRD and because CKD epidemiology in sub-Saharan Africa differs from that observed in other regions [16], it is conceivable that risk factors for proteinuria and renal disease among Black Africans might be different. Reasons of these differences are unclear but might be due to genetic and environmental differences.

Well-designed surveys taking benefit of the World Kidney Day (WKD) can serve as a framework for advocacy and community mobilization as well as an opportunity to offer voluntary mass screening to early detect CKD and its associated risk factors [17].

In the present study, we took advantage of the 2007 WKD to describe the prevalence of proteinuria and the number of subjects needed to screen to identify 1 person with proteinuria as well as to evaluate factors associated with proteinuria in the Congolese population.

Material and Methods

Study Design and Recruitment of Participants

Adults living in Kinshasa, a city of about 10 million inhabitants, were eligible for the 2007 WKD cross-sectional screening for CKD and associated risk factors if they were aged 12 years or older and if they were able to give oral informed consent. The population was informed about the study via community advertisement (TV, radio, newspapers, posters and word-of-mouth) as well as through community and political leaders.

Study Setting, Overview of Procedures and Data Collection

In order to get a large sample nonrepresentative of the adult population living in the city, study sites were selected arbitrarily in different quarters of the city. Those included the University of Kinshasa, the Pax private clinic near a very big bus station at Rond Point Ngaba (North), a secondary school, the Kabalo school in Kintambo (West), a church at Matonge, Saint Joseph, the central part of the city (Center) and a church at Kimbanseke, Saint Boniface (East).

The survey was conducted in March 2007 during 4 consecutive Thursdays from 8 a.m. to 6 p.m. by 75 trained volunteers recruited among medical doctors, laboratory technicians, nurses and medical students.

The subsequent phases of this work are illustrated in figure 1. In brief, the campaign included the following steps: educational message about the kidney (role, diseases and risk factors), registration, recording of general information (family and personal medical history, lifestyle habits), urinalysis, physical examination, blood sugar analysis, interpretation of the results and management.

Knowing that 12.4% of adults have CKD of all stages in Kinshasa [18], approximately 3,129 subjects were needed to reach this prevalence with error estimate of 2%. Of an intended sample size of three thousand five hundred, 3,134 persons agreed to participate. Among them, 3,018, aged 12 years or more completed the interview and were physically examined.

Interviews collected information on demographic characteristics, daily intake of salt and fruits and vegetables in the diet, smoking habit, alcohol consumption, indigenous herbal remedies use, birth weight knowledge and physical activity. The physical activity during the time of leisure was classified as activity (physical activity of at least 30 min/day or 4 h/week) and inactivity in the contrary case. Data about family and medical history of kidney disease, hypertension, diabetes, obesity as well as current treatment were recorded. They were asked to collect a urine sample which was then used to detect proteins with urinary strips (Medi-Test Combi 9) by the readers trained for this purpose. Female subjects were instructed to void a random urine specimen, remote from menstrual periods. Proteinuria was defined as 1+ or greater. For subjects having leukocyturia or positive dipstick nitrite test, classification as having proteinuria required its confirmation after treatment with antibiotics.

Body weight, height and waist/hip circumference were measured. Height was taken to the nearest 0.1 cm with a portable stadiometer (Seca) and weight was measured to the nearest 0.1 kg on a mechanical scale (Seca).

Thereafter, the subjects were allowed to relax for 5 min in a sitting position before determination of blood pressure. Blood pressure was measured twice in the right or left arm using an au-

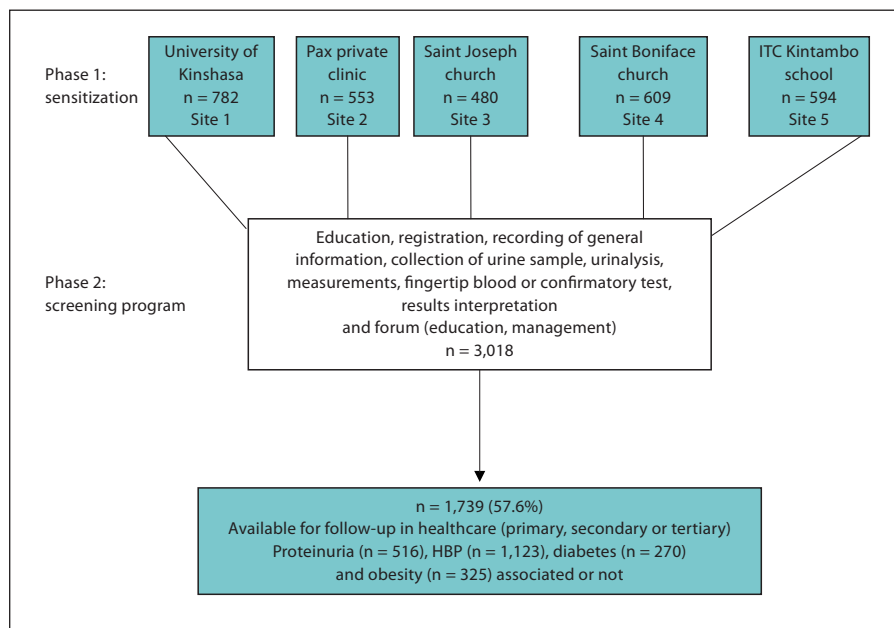


Fig. 1. Illustration of the phases of the free mass screening of proteinuria and associated risk factors of CKD at the 2007 WKD ('Are Your Kidneys OK') in Kinshasa. HBP = High blood pressure.

tomatic machine (Omron M 5-1) at heart level. Hypertension was defined by an average of systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg and/or concomitant use of antihypertensive medications by self-report (known hypertensive) [19].

The body mass index (BMI) was calculated from the measured height (in meters) and weight (in kilograms) and was categorized as not obese (<25), overweight ($25-29.9$) or obese (≥ 30) according to the 2000 WHO criteria [20]. Metabolic syndrome was defined simply as abdominal obesity (waist circumference >102 cm for males and >88 cm for females) associated with blood pressure $\geq 130/85$ mm Hg and fasting glucose ≥ 110 mg/dl [21].

Fingertip blood (Ascensia Entrust glucometer; Bayer) for fasting glucose or random glucose was also performed. The diagnosis of diabetes was confirmed after repeat testing on a subsequent week (fasting glucose values of ≥ 126 mg/dl) or a positive history of diabetes and/or concomitant use of antidiabetic medications by self-report (known diabetic) [22].

Kidney damage was defined as the presence of $\geq 1+$ protein (equivalent to ≥ 30 mg/dl).

Statistical Analysis

Results are presented as numbers, percentages or means \pm SD. Two-sample Student's t test and χ^2 test were used for comparison of means and proportions where appropriate. The crude (unadjusted) and adjusted odds ratios (OR) were estimated to assess the relationship between the risk factors and kidney damage (proteinuria) using a stepwise logistic regression analysis. The exposure variables included age, gender, smoking, alcohol consumption, indigenous herbal remedies, birth weight knowledge, family history (diabetes, hypertension, obesity and kidney disease), diabetes, hypertension and BMI. All data analysis and calculations except the χ^2 test were performed by using the standard statistical package (SPSS, version 13.0). χ^2 test was performed in

the dialog box using Medcalc, version 9.1.01. The zero hypothesis was rejected at $p < 0.05$.

All rules of confidentiality were complied with, including collection of information and physical examination. The study protocol and related documents were approved by the provincial and national levels of the Ministry of Health.

Results

Characteristics of the Study Population

More than half (57.6%) of the examined subjects had at least 1 of the signs of NCD (fig. 1). Table 1 shows the sociodemographic characteristics of the participants. The age range was 12–85 years (mean 44.3 ± 15.3 , median 45). Some statistically significant differences between male and female subjects were observed. Female subjects were older (mean 46.5 ± 14.8 vs. 42.8 ± 15.5 years, $p < 0.001$). Physical inactivity and a family history of obesity were more frequent among them than in male subjects. In contrast, proportions of those with low or high birth weight, smoking habit, herbal remedies use, high educational level and employment were more prevalent in male than in female subjects ($p < 0.01$).

Prevalence of Proteinuria and Number Needed to Screen to Identify One Person with Findings

Proteinuria (regardless of kidney function) was detected in 17.1% (95% CI 15.8–18.6) of participants but

Table 1. Characteristics of the study population by gender

Clinical features	Males (n = 1,767)	Females (n = 1,239)	p value
Age	42.8 ± 15.5	46.5 ± 14.8	<0.001
Age range, years			
12–29 years	527 (29.8)	237 (19.2)	<0.0001
30–44 years	445 (25.2)	262 (21.2)	0.01
45–56 years	375 (21.2)	375 (30.4)	<0.0001
57–85 years	420 (23.8)	333 (27)	0.05
Low or high birth weight ¹	253 (22.9)	151 (19.6)	0.03
History of hypertension	235 (13.3)	304 (24.7)	<0.0001
Detection rate of hypertension	384 (21.7)	199 (16.1)	0.0002
History of diabetes mellitus	78 (4.4)	54 (4.4)	0.9
Detection rate of diabetes	58 (3.2)	80 (4.1)	0.2
Smoking currently	213 (10.3)	23 (1.8)	<0.0001
Alcohol consumption currently	886 (50.1)	366 (29.5)	<0.0001
Herbal remedies use currently	655 (37.4)	335 (27.6)	<0.0001
Physical inactivity	432 (26.2)	536 (46.8)	<0.0001
Family history of hypertension	109 (6.2)	94 (7.7)	0.1
Family history of diabetes mellitus	430 (25.6)	279 (24.1)	0.3
Family history of obesity	301 (17.5)	297 (25.1)	<0.0001
Lack of employment	963 (54.5)	923 (74.8)	<0.0001
High educational level	1,075 (60.8)	304 (24.6)	<0.0001

Values expressed as numbers and percentages in parentheses or means ± SD, as appropriate. Data from the 2007 WKD ('Are Your Kidneys OK') in Kinshasa. ¹ Low birth weight: <2.5 kg; high birth weight: ≥3.8 kg.

only 21 (4%) were aware of their condition. The frequency distribution of dipstick proteinuria without hematuria is given in table 2. Among subjects with proteinuria, 15.3% (n = 463) of the total population exhibited isolated proteinuria and the remaining 1.7% (n = 53) of the study population had proteinuria with hematuria. Isolated hematuria, defined as dipstick hematuria ≥1+, was found in 3.8% (n = 114) of the total population.

In addition, the prevalence of proteinuria among other CKD risk factors screened is shown in figure 2. Furthermore, the prevalence of various states of proteinuria in 7 different target groups (whole population, diabetics, hypertensives, metabolic syndrome cases, obese, overweight subjects and persons without NCD) for 7 age categories (12–21, 22–31, 32–41, 42–51, 52–61, 62–71 and ≥72 years of age) is displayed in table 3. The prevalence estimates are also presented as the number of persons one would need to screen (number needed to screen to identify 1 participant with the constellation of findings specified in table 3). Overall, proteinuria becomes more prevalent with older age in most different target groups and the number needed to screen is lower.

Table 2. Distribution of degree of proteinuria of study population (n = 3,018)

Proteinuria	n	%
+1 (30 mg/dl)	449	14.8
+2 (100 mg/dl)	53	1.7
+3 (500 mg/dl)	14	0.4
All patients (≥+1)	516	17.1

Data from the 2007 WKD ('Are Your Kidneys OK') in Kinshasa.

Determinants of Proteinuria

Risk factors associated with proteinuria are summarized in table 4. Diabetes mellitus (adjusted OR 1.3, 95% CI 1.02–1.8; p < 0.05), overweight (adjusted OR 1.2, 95% CI 1.02–1.6; p < 0.05) and increasing age (adjusted OR 1.4 for over 50 years vs. <50 years, 95% CI 1.1–1.7; p = 0.01) were independent factors associated with proteinuria. The OR for proteinuria increased proportionately with age (data not shown). However, male gender, family and

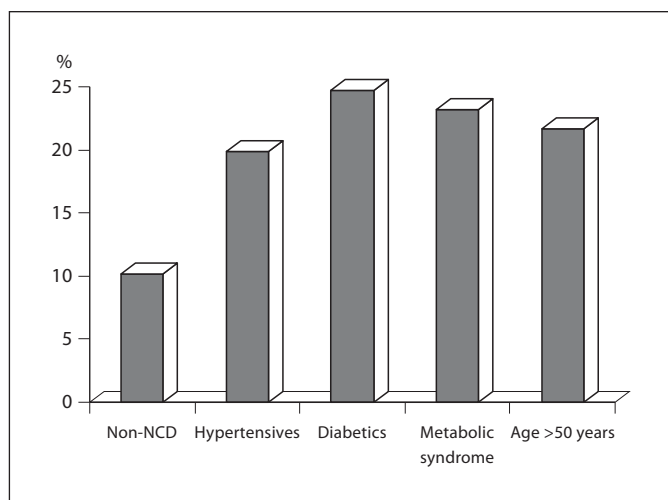


Fig. 2. Prevalence of proteinuria in non-NCD persons, hypertensives, diabetics, metabolic syndrome subjects and participants >50 years. Data from the 2007 WKD ('Are Your Kidneys OK') in Kinshasa.

medical history of kidney disease, hypertension or diabetes, smoking and herbal remedies use were not significant predictors for the presence of proteinuria in this study.

Discussion

A call to action on the 2007 WKD [17] prompted us to identify that a significant number of the adult population of Kinshasa has proteinuria and other CKD risk factors such as hypertension, diabetes and/or obesity. This fact is well illustrated by our recent report of increasing number of CKD and associated risk factors in the general population of Kinshasa [18].

Over 15% of our study subjects had proteinuria. This value is much higher than the 11% found in Bolivia [5] and the 8.7% in NHANES III [3], but lower than the 55, 35 and 26% observed in Tiwi islanders [23], South Africans [24] and among Zuni Indians [25], respectively. This

Table 3. Prevalence of proteinuria in 7 study groups by age (in decades)

	Age group, years							Total
	12-21	22-31	32-41	42-51	52-61	62-71	≥72	
Whole population								
Proteinuria	114 (8.7)	715 (11.4)	493 (18.6)	602 (18.2)	613 (18.9)	405 (22.4)	76 (19.7)	3,018 (17.1)
NNS	11	9	5	5	5	4	5	
Diabetics								
Proteinuria	5	31 (12.9)	36 (27.8)	50 (28)	82 (28)	59 (25.4)	7 (14.3)	270 (24.8)
NNS		8	4	4	4	4	7	4
Hypertensives								
Proteinuria	14	86 (11.6)	103 (10.7)	246 (18.7)	348 (20.1)	260 (28.5)	66 (19.7)	1,123 (19.9)
NNS		9	9	5	5	4	5	5
Metabolic syndrome								
Proteinuria		9 (1.1)	11 (9.1)	51 (19.6)	57 (28.1)	25 (20)	6 (50)	159 (22.6)
NNS		9	11	5	4	5	2	4
Obese								
Proteinuria	1	27 (7.4)	40 (15)	96 (25)	97 (25.8)	43 (16.3)	8 (37.5)	312 (21.4)
NNS		14	7	4	4	6	3	5
Overweight								
Proteinuria	8 (12.5)	60 (15)	90 (23.3)	172 (19.8)	182 (19.2)	87 (33.3)	8 (25)	607 (21.6)
NNS	8	7	4	5	5	3	4	5
Non-NCD								
Proteinuria	93 (8.6)	538 (10.4)	318 (13.5)	281 (10.3)	199 (9.0)	107 (14)	20 (10)	1,556 (10.9)
NNS	12	10	7	10	11	7	10	9

Values expressed as numbers and percentages in parentheses. NNS = Number needed to screen.

Table 4. Determinants of proteinuria (univariate and multivariate analysis)

Risk factors proteinuria (Medi-Test Combi 9)	Univariate analysis			Multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
Hypertension vs. no	1.3	1.1–1.6	0.001	1.07	0.8–1.3	0.5
Diabetes vs. no	1.5	1.1–2.1	0.003	1.3	1.02–1.8	0.03
Overweight vs. no	1.3	1.1–1.7	0.005	1.2	1.02–1.6	0.03
Metabolic syndrome vs. no	1.5	1.03–2.2	0.03	1.4	0.9–2.1	0.1
Age <50 vs. ≥50 years	1.5	1.2–1.8	0.000	1.4	1.1–1.7	0.002

discrepancy between studies may be due partly to various definitions (microalbuminuria vs. dipstick proteinuria) and criteria of selection (random vs. without random sample or/and high risk population vs. whole population) applied in each survey.

We recognize that dipstick proteinuria has limited sensitivity and specificity [26]. However, despite the fact that the present study used dipstick proteinuria, it is of great prognostic value. For example, screening with the urine dipstick test for proteinuria has been used successfully in Japan since 1972, targeting every child and worker, as well as since 1983 for every resident over 40 years old [27]. Moreover, a survey undertaken in Okinawa after 17 years of follow-up indicates that individuals with dipstick-positive proteinuria are at increased risk of developing CKD, in fact in proportion to the severity of proteinuria [28]. Sam et al. [29] have demonstrated that trace dipstick proteinuria usually means microalbuminuria. Indeed, in their survey, a negative urinalysis for proteinuria excluded microalbuminuria in 87% and proteinuria in 78% of cases. In addition, more recently, it has also become apparent that dipstick proteinuria is more indicative of microalbuminuria than macroalbuminuria [30]. This is a fact because of the subjects that were trace, 1+ or 2+ positive on a dipstick protein, 61, 71 and 41%, respectively, had microalbuminuria, whereas only 1, 7 and 50%, respectively, had macroalbuminuria. It is likely that the majority of our cases that were positive for proteinuria in fact had microalbuminuria.

In our study, 9 adults that do not have NCD need to be screened to identify 1 individual with proteinuria. This number decreases in certain subgroups, amounting to 4 in diabetics, 5 in hypertensives, 4 in persons with metabolic syndrome or 5 in persons >50 years. The NHANES III yielded similar results [14] especially in the diabetic group. Yet, some differences exist between the 2 studies. The testing method for albuminuria was different. In addition, it is possible that the relatively low prevalence of

albuminuria observed in their survey [14] compared to ours results from the use of antihypertensive therapy (specifically, angiotensin-converting enzyme inhibitor and angiotensin receptor blocker use), which may reduce the number of patients with proteinuria.

In our present survey, diabetes, overweight and increasing age were independently associated with the presence of proteinuria. Age is a recognized risk factor for renal disease [31]. This is attributed partly to glomerular obsolescence and decreased renal vascular flow [32]. Other factors associated with proteinuria in univariate but not in multivariate analysis in our study were hypertension and metabolic syndrome. Several studies already demonstrated the relationship between hypertension as well as increasing BMI and proteinuria [33]. For example, in prospective studies, such as the Multiple Risk Factor Intervention Trial (MRFIT), each 9-mm Hg increase in DBP was associated with an OR of 1.37 for the presence of dipstick-positive proteinuria [34]. Plausible mechanisms have focused on the elevation in the pressure transmitted to glomeruli, which might result in sclerosis and proteinuria [35]. Moreover, as reported by Chen et al. [36], metabolic syndrome is associated with higher risk for proteinuria. We have confirmed this. The exact mechanism of this proteinuria/albuminuria-associated cardiovascular risk remains unknown, but might be due to endothelial dysfunction [37].

However, some risk factors for proteinuria such as family and medical history of kidney disease, low birth weight and smoking, reported elsewhere [15, 38], were not observed in the present study. The lack of awareness of renal disease by both health workers and lay population can partly explain this observation. Indeed, in our study, a little more than three quarters of the population does not know the localization, role or even name of the kidney in their mother tongue. In addition, most of our study population did not have birth certificates or knowledge of their weight at birth. The reason why tobacco was

not associated with proteinuria remains unclear and deserves further study.

Strength and Limitations of our Study

The strength of this study is that it includes a large sample of the general population of Kinshasa and that we used standardized methods of data collection. Already, by doing this study, we have improved awareness of CKD in the DRC and also addressed the fear of disease surveillance formerly observed in this population.

However, there are some limitations and constraints that must be considered. First, a selection bias may exist because subjects who volunteered to participate in the screening program might be more likely to have the risk factors that we studied, including proteinuria. Second, as in any cross-sectional study, causation cannot be established because the sequence of events between exposure and outcome is not defined. Third, because of lack of resources, our study used simply dipstick methods to screen for proteinuria, which has detection limits as mentioned earlier [26]. Indeed, common causes [26, 39] for false positives by dipstick test may be seen in patients with gross hematuria, contamination with antiseptic agents (chlorhexidine, benzalkonium chloride), alkaline urine pH, highly concentrated urine and, conversely, false negatives may occur in patients with dilute urine or in disease states in which predominant protein is not albumin (dipstick protein being sensitive only to albumin). In addition, proteinuria can occur transiently in response to hemodynamic stress (severe exercise, fever and convulsion), dehydration, cold exposure, congestion heart failure, urinary tract infection and during menstruation or pregnancy in women [40]. It is also likely that some positive proteinuria among subjects with neither hypertension nor diabetes might be due to chronic glomerulonephritis which remains a major cause of ESRD in the DRC [6, 41]. Furthermore, some cases of proteinuria in this study might be due to HIV or hepatitis B or C virus infections which are prevalent in this country [41]. Yet, this study did not address the specific causes of proteinuria in individual subjects. Consequently, the only sign of CKD for those subjects at early stage is urinary abnormalities.

Fourth, except for proteinuria associated with pyuria, indicators of kidney damage were defined based on a single measurement. In K/DOQI [42] and K/DIGO [2] guidelines, the definition of CKD requires the persistence of kidney damage for at least 3 months. Also, studies based on NHANES III indicate that in repeated measurement, only 63.2% of those with albuminuria would have persistently positive results [3]. Hence, the single

measurement of proteinuria in our study might overestimate its prevalence.

Fifth, distribution of proteinuria across categories of estimated GFR could be informative and very useful. Unfortunately, we have not measured serum creatinine in this study due to pragmatic and economic reasons. However, proteinuria remains a good risk marker for developing ESRD [27].

To conclude, the present work, despite possible methodological limitations, emphasizes that proteinuria and CKD risk factors such as hypertension, diabetes and obesity are highly prevalent in Kinshasa, while awareness of NCD is very low. This study confirms diabetes, overweight and age as the strongest independent risk factors associated with proteinuria. Also, prevalence of proteinuria among subjects with neither diabetes nor hypertension is high as in Japan [27] but not in Caucasian populations. If confirmed, these data support the idea that annual urinalysis screening for the whole population in the DRC might be cost-effective. This is in contrast to the report of Boulware et al. [43] who affirm that annual screening for proteinuria in US adults was not cost-effective because the prevalence of proteinuria was very low. Furthermore, urinary albumin and creatinine ratio testing as well as microalbuminuria are more expensive than dipstick proteinuria. Therefore, urine dipstick test for proteinuria is suitable as a first step for most countries or races that have a high prevalence of proteinuria such as the DRC. Further studies to assess the performance of dipstick proteinuria as well as its cost-effectiveness analysis and including estimated GFR in this country are needed to develop adapted preventive strategies. This targeted prevention strategy could result in the reduction of cardiovascular events as well as the alarming incidence of ESRD.

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