High prevalence of undiagnosed chronic kidney disease among at-risk population in Kinshasa, the Democratic Republic of Congo

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Abstract

Background: There is limited knowledge of Chronic Kidney Disease (CKD) among high risk populations, especially in the developing countries. We report our study of testing for CKD in at-risk subjects.

Methods: In a cross-sectional study, 527 people from primary and secondary health care areas in the city of Kinshasa were studied from a random sample of at-risk out-patients with hypertension, diabetes, obesity, or HIV+. We measured blood pressure (BP), blood glucose level, proteinuria, body mass index, and estimated glomerular filtration rate (eGFR by MDRD equation) using calibrated creatinine levels based on one random measurement. The associations between health characteristics, indicators of kidney damage (proteinuria) and kidney function (<60 ml/min/1.73 m²) were also examined.

Results: The prevalence of CKD in this study was 36%, but only 12% were aware of their condition. 4% of patients had stage 1 CKD, 6% stage 2, 18% stage 3, 2% stage 4, and 6% had stage 5. 24 hour quantitative proteinuria (>300 mg/day) was found in 19%. In those with the at-risk conditions, the % of CKD was: 44% in patients with hypertension, 39% in those with diabetes; 16% in the obese and 12% in those who were HIV+. 82% of those with a history of diabetes had elevated serum glucose levels at screening (≥126 mg/dl). Only 6% of individuals with hypertension having CKD had reduced BP to lower than 130/80 mmHg. In multivariate analysis, diabetes, proteinuria and hypertension were the strongest determinants of CKD 3+.

Conclusion: It appears that one out of three people in this at-risk population has undiagnosed CKD and poorly controlled CKD risk factors. This growing problem poses clear challenges to this developing country. Therefore, CKD should be addressed through the development of multidisciplinary teams and improved communication between traditional health care givers and nephrology services. Attention to CKD risk factors must become a priority.
Background
Chronic Kidney Disease (CKD) is a worldwide health problem [1]. Indeed, the incidence and prevalence of CKD has increased in recent years in both developed and developing countries [2] including in Sub-Saharan Africa (SSA) [3]. In SSA, CKD affects mainly young adults in their productive years and is a significant cause of death [3,4]. This may occur by death from kidney failure, and also by cardiovascular deaths, which are increased in those with CKD. Major contributory factors for this ominous picture include late referral to hospital, limited renal replacement therapy (RRT), limited capacity of health workers for CKD detection and prevention, and poor awareness of kidney disease in the community [3,5,6].

This situation prompted the International Society of Nephrology Commission for the Global Advancement of Nephrology (ISN COMGAN) to make the fight against CKD one of its priorities, by promoting awareness, early detection, and effective treatment [7].

In our recent survey [4] in the general population of Kinshasa, the capital of the Democratic Republic of Congo (DRC) the prevalence of early stage CKD was 10 times greater than that of stage 5 CKD or end stage renal disease (ESRD). Thus, while severe CKD can result in progressive kidney failure, the effects of less-severe CKD are quantitatively more important. Although cumulative evidence shows that early detection and treatment prevents or delays some of its adverse outcomes [8-11], the majority of subjects at early stages of CKD are undiagnosed and under-treated in SSA [6]. Indeed, because of the scarcity of financial resources and shortage of manpower, CKD prevention programs are either rudimentary or virtually nonexistent in the developing world [12].

Furthermore, attention to health problems in SSA is usually been focused on infectious diseases, rather than on chronic non-communicable disease (CND) such as CKD.

Screening of specific groups for CKD, such as those with known diabetes (DM) or with hypertension (HTN), may be more cost effective than screening the general population [13]. But, the benefits of targeted screening of patients with DM and HTN versus screening of general population are debatable [14]. A non validated Modification of Diet in Renal Disease (MDRD) study equation in Black Africans, would probably lead to an over or under-estimation of CKD prevalence in Sub-Saharan population.

Nonetheless, since we found an increasing prevalence of CKD risk factors such as HTN, DM, and obesity in Kinshasa [4], along with the co-occurrence of human immunodeficiency virus (HIV) infection and HIV-associated renal diseases [15], it seemed reasonable to target screening on these groups [16]. The objective of this survey was to experiment early detection of a large numbers of previously unidentified persons with or at high risk for CKD. In addition, we determined the prevalence of CKD across selected risk factors and according to the level of kidney function within groups. Finally, socio-demographic features and clinical parameters of this at-risk group were assessed.

Methods
Study design and population
The present cross-sectional study is the second part of a larger ongoing study of CKD and associated risk factors termed "Prévalence, détection précoce et prévention des maladies rénales chroniques et facteurs de risque associés (PDMRA) en République Démocratique du Congo ". The present survey was done between January 9 and May 25, 2007.

Screening sites included primary (n = 9) and secondary health care (n = 4) chosen at random among networks of healthcare areas existing in the city of Kinshasa. The choice of the networks was based on the following criteria: a high number of the patients at-risk of CKD attending the centre, agreement of the authorities and availability of the health workers in these centres to select the subjects as well as to accommodate the research workers. PDMRA screening was conducted by a mobile research team composed of nephrologists, nurses and laboratory technicians. Primary care is a term used to define the activity of a health care provider who acts as a first point of consultation for all patients, while secondary health care includes dispensation of the care, hospital admissions and quality control of the structures of primary care.

Eligibility criteria for screening were age of 18 years or older and a personal history of HTN, DM, obesity or HIV infection, or first degree relative with kidney disease.

Screening Examinations and data collection
Knowing that 12.4% of adults have CKD in Kinshasa [4], approximately 473 subjects were required to reach that prevalence with error estimate of 3% [17]. Of an intended sample size of 550, 527 persons (291 in primary care and 236 in secondary care) agreed to participate. But, for three of them, the sample of serum was not properly handled.

All participants provided informed written consent before enrolment. They were examined by the research team, which recorded information on demographics, diet, smoking, alcohol consumption, use of indigenous herbal drugs, and birth weight knowledge. Data about first degree family relatives and medical history for kidney disease, HTN, DM and current treatment were also recorded.
Body weight, height and waist circumference were measured. HTN, DM, obesity and HIV infection had been diagnosed during past patient visits. These diagnoses were confirmed in writing. All HIV participants except twelve received standard weight-based dosages of highly active antiretroviral therapy (HAART), but medications were not adjusted for kidney function. They were initiated on stavudine plus lamivudine with either nevirapine (82%) or efavirenz (4%).

Blood pressure (BP) was measured twice in the right or left arm using a calibrated sphygmomanometer (WelchAllyn, Germany) at heart level. The subjects were allowed to relax for 5 minutes in a sitting position before determination of blood pressure.

HTN was defined as a systolic blood pressure $\geq 140$ mmHg or diastolic blood pressure $\geq 90$ mmHg and/or concomitant use of antihypertensive medications by self-report [18].

BP was categorized according to the Seventh Joint National Committee Report on Detection, Evaluation and Treatment of High Blood Pressure [18]. The categories were as follows:

- normal, $< 120$ and $< 80$ mmHg,
- prehypertension, $120–139$ or $80–89$ mm Hg;
- stage 1, $140–159$ or $90–99$ mm Hg;
- stage 2, $\geq 160$ or $\geq 100$ mm Hg.

The body mass index was calculated from the measured weight (in kilograms) and height (in meters) and was categorized as not obese ($< 25$ kg/m$^2$), overweight ($25$ to $29.9$ kg/m$^2$) or obese ($\geq 30$ kg/m$^2$) according to the 2000 WHO criteria [19].

The diagnosis of DM was established after two fasting glucose values of $\geq 126$ mg/dl using fingertip blood (Accutrend glucometer) and/or concomitant use of antidiabetic medications. DM was classified as type 2 or type 1 by clinical features as follows. Illness starting after age 40 years, the presence of chronic complications at onset, and an absence of ketones determined the diagnosis of type 2 diabetes. On the other hand, illness onset before or at age 30, and typical clinical signs (weight loss, asthenia, polyuria, polydipsia) determined the diagnosis of type 1 diabetes.

The participants provided a urine sample to detect proteins by urinary strips ('Combur 7-test'). Female subjects were instructed to void a random urine specimen, remote from menstrual periods. If positive with dipstick protein of 3+ ($n = 102$), measurement of 24-hour urinary protein was obtained ($n = 99$). Because ratio of albumin to creatinine (ACR) was not available and because urine dipstick provides only a semi-quantitative estimation of proteinuria and has imperfect accuracy in diagnosis of persistent proteinuria, kidney damage in stage 1 and 2 CKD in our study was identified as 24-hour urinary protein $\geq 300$ mg per day. Serum creatinine and 24-hour quantitative proteinuria were carried out according to the kinetic Jaffe (semi-automated polyphotometer Visual Biomérieux) and Esbach methods, respectively. These tests were performed in the laboratory of the Belgian medical centre of Kinshasa "CMK". For estimated Glomerular Filtration Rate (eGFR) determination, the abbreviated equation from the MDRD study was used. We calibrated the creatinine results measured with the Jaffe method against a traceable isotope dilution mass spectrometry (IDMS) enzymatic method (creatinine +, Roche enzymatic diagnostics) as described [4]. Recalibrated serum creatinine values were thereafter computed for each participant and the new MDRD study equation was used for estimation of the eGFR as $175 \times (\text{serum creatinine level} [(\text{mg/dl})]^{1.154} \times (\text{age} [(\text{years})])^{0.203}$ [20]. For women and for blacks (all patients in our study), the product of this equation was multiplied by correction factor of 0.742 and 1.21, respectively.

The K/DOQI guidelines [21] for definition and classification of CKD were used in the present study. The CKD stages are defined as follows: stage 1, proteinuria $\geq 300$ mg per day with an eGFR higher than 90 ml/min/1.73 m$^2$; stage 2, proteinuria $\geq 300$ mg per day with an eGFR of 60 to 89 ml/min/1.73 m$^2$; stage 3, an eGFR of 30 to 59 ml/min/1.73 m$^2$; stage 4, an eGFR of 15 to 29 ml/min/1.73 m$^2$; and stage 5, an eGFR $< 15$ ml/min/1.73 m$^2$.

The term chronic renal failure or CKD 3+ refers to an eGFR $< 60$ ml/min/1.73 m$^2$. The term "all stages of CKD" includes both kidney damage (early stage of CKD, 1 and 2) and chronic renal failure (CKD 3 or worse).

**Statistical analysis**

Results are presented as number and percentage or mean ± SD. 2-sample Student’s t test and chi-squares were used for comparison of means and proportions, where appropriate.

The outcome under analysis was the presence of CKD, defined as above. Exposure variables that were considered included gender, age, smoking, herbal drugs use, BMI, DM, pulse pressure, family history of kidney disease (FHKD), HTN, and HIV infection. The crude (unadjusted) relationships between the exposure variables and the presence or absence of CKD were examined in univariate logistic regression analyses. Multivariate stepwise logistic
regression analysis was then done to evaluate the simultaneous effects of various exposure variables, with adjustment for the potential confounding effects of other factors. The above approaches were applied separately for CKD stage 3+ and for proteinuria.

A multiple linear regression model was used to determine the independent association between the reduction of an eGFR < 60 ml/min/1.73 m² and continuous variables such as age, duration of DM, duration of HTN, BP, and BMI. Except chi-squares, all data analysis and calculations were performed by using a standard statistical package (SPSS Inc, Chicago, IL version 13.0, 2004). Chi-squares were made in the dialog box using medcalc version 9.1.01, 2005. A P value < 0.05 indicated statistical significance. All rules of confidentiality were complied with, including collection of information and physical examination. This study was approved by ethics committee of the Provincial Medical Inspection of Kinshasa.

Results
A. Characteristics of the study population
Sociodemographic characteristics of the participants are listed in Table 1. The age range was between 18–90 years old (mean 54 ± 15, median 55). Some statistically significant differences between male and female subjects were observed.

B. CKD according to health care level
The overall prevalence of CKD stage 1–5 was 36% (95% CI, 36.0 to 36.4) (Table 2) and was higher in males than in females, being 40% versus 34%, respectively. Of these 190 subjects with CKD, 14% had reduced eGFR MDRD equation < 60 ml/min/1.73 m² (CKD stage 3 or more). However, only twenty four of those with CKD (12%) were aware of their condition. 24 h quantitative proteinuria ≥ 300 mg was detected in 19% of the studied population. Although all stages of CKD were found in both levels of health care, 9 patients (3%) and 24 patients (8%) in primary care and, 13 patients (6%) and 8 patients (3%) in secondary care had CKD stage 1 or 2, respectively. Thus, CKD stage 2 was more prevalent in primary care compared to secondary care (P < 0.05). In contrast, CKD stage 4 and 5 was more frequent in secondary health care than it was in primary care (P < 0.001). Most of patients with stage 5 CKD died quickly from uraemia because of lack of dialysis.

In addition, the prevalence of CKD among subjects at-risk according to K/DOQI stage is shown in figure 1. In those with the at-risk conditions, the prevalence of CKD was: 45% in patients with DM and HTN, 26% in patients with HTN, 16% in the obese and 12% in those who were HIV+. In persons having FH-KD, CKD was found in 8%. Table 3 shows the 24-hour quantitative urine protein, dipstick abnormalities in the urine (proteinuria, pyuria and haematuria) and elevated creatinine (men > 1.6 mg/dl and women > 1.4 mg/dl) according to K/DOQI stage.

In the 82 people with HIV, quantitative proteinuria at more than 300 mg/day was observed in five subjects; five others had CKD stage 3+.

Table 1: Population characteristics.

| Clinical features       | Males N = 229 | Females N = 298 | Total N = 527 | P  |
|------------------------|---------------|-----------------|--------------|----|
| Age mean ± SD (yr)     | 55.3 ± 15.3   | 52.8 ± 14.9     | 53.9 ± 15.5  | 0.05|
| Age range n (%)         |               |                 |              |
| -18 to 43 yr            | 53 (23.1)     | 83 (27.9)       | 136 (25.8)   | 0.25|
| -44 to 55 yr            | 52 (22.7)     | 83 (27.9)       | 135 (25.6)   | 0.20|
| -56 to 67 yr            | 69 (30.1)     | 78 (26.2)       | 147 (27.9)   | 0.37|
| -> 67 yr                | 55 (24.0)     | 54 (18.1)       | 109 (20.7)   | 0.12|
| Hypertension n (%)      | 129 (56.3)    | 175 (58.7)      | 304 (58.2)   | 0.62|
| Diabetes n (%)          |               |                 |              |
| - Type 1                | 125 (54.5)    | 162 (54.4)      | 287 (54.5)   | 0.76|
| - Type 2                | 8 (6.4)       | 6 (3.7)         | 14 (4.9)     | 0.4 |
| Obesity n (%)           | 117 (93.6)    | 156 (96.3)      | 273 (95.1)   | 0.4 |
| HIV infection* n (%)    | 26 (32.4)     | 60 (49.6)       | 86 (43.4)    | 0.03|
| FH-KD first degree* n (%) | 18 (7.3)   | 25 (11.7)       | 38 (9.7)     | 0.12|
| History of Kidney disease n (%) | 15 (6.8) | 9 (3.1) | 24 (4.6) | 0.07|
| Smoking currently n (%) | 28 (12.3)     | 10 (3.4)        | 38 (7.3)     | 0.0002|
| Herbal remedy use n (%) | 52 (25.4)     | 37 (12.5)       | 89 (18.2)    | 0.0002|
| Low educational level** | 65 (29.0)     | 162 (55.5)      | 227 (44.0)   | < 0.0001|

Values expressed as numbers and proportions in parentheses or mean ± SD, as appropriate.
SD, standard deviation. yr, years.
Percentages based on total participant number except for * HIV infection status or responding number.
** low level education (< 6 years).
C. Hypertension and/or Diabetes, and CKD status

Table 4 gives BP control according to JNC VII [18] and serum glucose levels of the participants according to their CKD status. CKD patients were much more likely to have HTN than those without CKD ($P = 0.0005$). 82% of participants with history of DM had elevated fasting serum glucose levels at screening ($\geq 126$ mg/dl [$\geq 7$ mmol/l]), and 78% of those with history of HTN did not have their BP controlled to less than 140/90 mmHg. Among individuals with HTN having CKD, 99% received treatment. However, only 6% of all individuals with HTN had their BP controlled to less than 140/90 mmHg. Among individuals with HTN having CKD, 99% received treatment. Furthermore, only 4% of patients with DM and HTN having CKD had BP controlled to less than 130/80 mmHg and ACEI treatment was prescribed in only 29%. Patients with DM were treated with insulin (53%), oral medication such as metformin or glibenclamide (41%) or insulin combined with oral antidiabetic medication (1%). Table 5 summarizes the current problems of CKD, ESRD, and cost.

D. Determinants of CKD

Determinants of CKD 3+ are displayed in Table 6. HTN (adjusted OR 3.3, 95% CI 1.7–6.5; $P < 0.001$), DM (adjusted OR 2, 95% CI 1.1–3.8; $P = 0.01$) and dipstick proteinuria (adjusted OR 2, 95% CI 1.1–3.6; $P = 0.02$) were independent factors associated with CKD 3+.

Table 2: Prevalence of CKD among at-risk population by level of health care.

| Stages of CKD/Health care (eGFR, ml/min/1.73 m²) | Primary N = 291 (%) | Secondary N = 236 (%) | Total N = 527 (%) | P |
|-----------------------------------------------|---------------------|-----------------------|-------------------|---|
| 1 (≥ 90)*                                    | 9 (3.1)             | 13 (5.5)              | 22 (4.2)          | 0.25 |
| 2 (60 to 89)*                                | 24 (8.3)            | 8 (3.4)               | 32 (6.1)          | 0.03 |
| 3a (45 to 59.9)                              | 43 (14.9)           | 21 (8.9)              | 64 (12.2)         | 0.05 |
| 3b (30 to 44.9)                              | 23 (8.0)            | 9 (3.8)               | 32 (6.1)          | 0.07 |
| 4 (15 to 29.9)                               | 1 (0.3)             | 9 (3.8)               | 10 (1.9)          | 0.007 |
| 5 (< 15)                                     | 2 (0.7)             | 28 (11.9)             | 30 (5.7)          | < 0.0001 |
| All stages of CKD                            | 102 (35.3)          | 88 (37.4)             | 190 (36.2)        | 0.68 |
| Proteinuria ≥ 300 mg/day                     | 52 (17.9)           | 47 (19.9)             | 99 (18.7)         | 0.6 |

Values expressed as numbers and proportions in parentheses or mean ± SD, as appropriate. Percentages based on responding number or total participant number. For three patients, the sample of serum was not properly handled (missing data).

* 24-hours urinary protein excretion ≥ 300 mg/day. eGFR based on MDRD study.

CKD is defined either as kidney damage (proteinuria ≥ 300 mg/day) and/or kidney function (< 60 ml/min/1.73 m²).

Table 3: Prevalence of abnormal urinary findings and serum creatinine by K/DOQI stage of CKD.

| Abnormalities/eGFR | < 15 N = 27 (%) | 15–29 N = 10 (%) | 30–59 N = 96 (%) | 60–89* N = 32 (%) | ≥90* N = 22 (%) |
|--------------------|----------------|-----------------|-----------------|-------------------|----------------|
| Dipstick proteinuria | 25 (92.6)    | 8 (88.9)        | 81 (85.3)       | 32 (100.0)        | 22 (100.0)     |
| Proteinuria ≥ 300 mg/day | 18 (66.7)   | 3 (33.3)        | 24 (25.3)       | 32 (100.0)        | 22 (100.0)     |
| Dipstick hematuria  | 9 (33.3)     | 3 (33.3)        | 11 (11.6)       | 7 (34.3)          | 3 (13.6)       |
| Dipstick pyuria     | 4 (14.8)     | 4 (44.4)        | 58 (61.0)       | 21 (65.6)         | 10 (45.4)      |
| S. creatinine (men >1.6 md/dl/women > 1.4 mg/dl) | 27 (100.0) | 10 (100.0) | 53 (55.2) | 1 (3.1) | 0 |

Values expressed as numbers and proportions in parentheses or mean ± SD, as appropriate.

* 24-hours urinary protein excretion ≥ 300 mg/day. eGFR based on MDRD study.

CKD is defined either as kidney damage (proteinuria ≥ 300 mg/day) and/or kidney function (< 60 ml/min/1.73 m²).

Percentages based on total number of dipstick proteinuria available (n = 521).

S. creatinine = serum creatinine; SD, standard deviation.
However, only pulse pressure > 60 mmHg (adjusted OR 1.8, 95% CI 1.03–3.2; \( P = 0.03 \)) was statistically associated with the presence of proteinuria in this study.

In patients with DM, increasing age and duration of DM were associated with reduction of kidney function (as eGFR MDRD equation < 60 ml/min/1.73 m²) in multiple linear regression models according to the following equation:

\[
\text{eGFR MDRD study equation} = 61.6 - 0.12 \times \text{age, in years} - 0.43 \times \text{diabetes duration, in years}, \quad P = 0.03.
\]

By contrast, in patients with HTN, no risk factors were associated with low eGFR in multiple linear regression models.

**Discussion**

This study documents CKD among at-risk population in the health system of Kinshasa, a large city in Sub-Saharan Africa. The overall prevalence of undiagnosed CKD is high, at 36%. This prevalence is probably not real since it was based on non validated MDRD study equation. However, we think that the question of the validity of eGFR MDRD in Black race is debatable. Indeed, since the MDRD Study formula has been adequately validated in African Americans with kidney disease \[22\], extrapolation to Black Africans may be justified in view of similar genetic and physical attributes. But, validation should still be carried out. Nevertheless, the value of 36% is almost triple the prevalence of CKD in the general population of this city \[4\]. Similar trend has been noted in the Kidney Early Evaluation Program (KEEP) study \[23\], mainly for CKD 3+. This fact supports the use of targeted screening in identifying large numbers of subjects at-risk for CKD. It also confirms that the risk factors for CKD that are encountered in developed countries are also found in developing Africa.
In addition, our survey indicates that one person out of five in this group has proteinuria, which was occurred at all stages of CKD. Among individuals classified as having CKD stage 3, 25% had macroproteinuria. As some authors [14,24,25] have suggested, those subjects are the groups at most risk for cardiovascular disease (CVD) and CKD progression. With proteinuria and eGFR measurements, we have identify individuals with CKD stage 1 (4% of studied population) and CKD stage 2 (6%). In fact, identifying individuals with these earlier stages is of utmost importance since strong evidence emerge that the renal and cardiovascular risks that are associated with stage 1 and 2 are nearly equal to those of stage 3 [14]. Regrettably, in spite of this prevalence of proteinuria, in most cases it was neither detected earlier nor correctly managed before this study was done. Indeed, in almost all centres, 24 hour-quantitative proteinuria or dipstick proteinuria were not routinely available outside this study. Qualitative proteinuria was carried out in usual practice using the acetic acid method, which has limits of sensitivity and specificity.

Table 4: Hypertension and/or diabetes, and CKD status.

| Clinical features | CKD patients | Non CKD patients | Total | P |
|-------------------|--------------|------------------|-------|---|
| **JNC 7 guidelines** |             |                  |       |   |
| All patients (BP in mmHg) |             |                  |       |   |
| Normal, < 120 and < 80 | 52 (27.5)   | 143 (43.2)       | 195 (35.5) | 0.0005 |
| PreHBP, 120–139 or 80–89 | 32 (16.9)   | 56 (19.6)        | 88 (16.9) | 0.5 |
| Stage 1, 140–159 or 90–99 | 38 (20.1)   | 72 (21.8)        | 110 (21.2) | 0.7 |
| Stage 2, ≥ 160 or ≥ 100 | 67 (35.4)   | 60 (18.1)        | 127 (24.4) | <0.0001 |
| **Hypertensives** |             |                  |       |   |
| Antihypertensive drugs |             |                  |       |   |
| none                | 1 (1.1)     | 11 (10.6)        | 22 (11.2) | 0.01 |
| Any treatment       | 89 (98.9)   | 93 (89.4)        | 182 (88.8) | 0.01 |
| 1 antihypertensive  | 62 (71.3)   | 60 (57.7)        | 122 (62.2) | 0.06 |
| mean antihypertensive drugs | 1.28 ± 0.5 | 1.22 ± 0.6 | 1.25 ± 0.6 | 0.1 |
| ACEI*               | 21 (23.3)   | 33 (31.7)        | 54 (27.7) | 0.2 |
| Normal, < 120 and < 80 | 7 (5.2)      | 17 (10.0)        | 24 (7.9) | 0.1 |
| High normal, 120–139 or 80–89 | 22 (16.4)   | 21 (12.4)        | 43 (14.1) | 0.4 |
| Stage 1, 140–159 or 90–99 | 38 (28.4)   | 72 (42.4)        | 110 (36.2) | 0.01 |
| Stage 2, ≥ 160 or ≥ 110 | 67 (50.0)   | 60 (35.3)        | 127 (41.8) | 0.01 |
| < 130/80            | 8 (6.0)     | 21 (12.4)        | 29 (9.5) | 0.09 |
| < 125/75            | 4 (3.0)     | 11 (6.5)         | 15 (4.9) | 0.2 |
| Serum glucose level (mg/dl) |             |                  |       |   |
| Diabetics |             |                  |       |   |
| < 110               | 14 (12.8)   | 17 (9.8)         | 31 (11.0) | 0.5 |
| ≥ 110–125           | 8 (7.3)     | 12 (6.9)         | 20 (7.1) | 0.9 |
| ≥ 126               | 87 (79.8)   | 145 (83.3)       | 232 (82.0) | 0.5 |
| ≥ 180               | 45 (41.3)   | 91 (52.3)        | 136 (48.1) | 0.09 |

Values expressed as numbers and proportions in parentheses or mean ± SD, as appropriate.
CKD is defined either kidney damage (proteinuria ≥ 300 mg/day) and/or kidney function (< 60 ml/min/1.73 m²). Percentages based on responding number, not total participant number.
ACEI: Angiotensin-Converting Enzyme Inhibitors. PreHTN = Prehypertension.

In addition, our survey indicates that one person out of five in this group has proteinuria, which was occurred at all stages of CKD. Among individuals classified as having CKD stage 3, 25% had macroproteinuria. As some authors [14,24,25] have suggested, those subjects are the groups at most risk for cardiovascular disease (CVD) and CKD progression. With proteinuria and eGFR measurements, we have identify individuals with CKD stage 1 (4% of studied population) and CKD stage 2 (6%). In fact, identifying individuals with these earlier stages is of utmost importance since strong evidence emerge that the renal and cardiovascular risks that are associated with stage 1 and 2 are nearly equal to those of stage 3 [14]. Regrettably, in spite of this prevalence of proteinuria, in most cases it was neither detected earlier nor correctly managed before this study was done. Indeed, in almost all centres, 24 hour-quantitative proteinuria or dipstick proteinuria were not routinely available outside this study. Qualitative proteinuria was carried out in usual practice using the acetic acid method, which has limits of sensitivity and specificity.

Table 5: Projected Annual cost arterial hypertension, Diabetes and ESRD Treatment.

| Medications | Cost per patient (US$) | Total cost of all patients projected (US$) |
|-------------|------------------------|------------------------------------------|
| Antihypertensive |                       |                                          |
| Thiazide diuretics | 100                    | 280 million                              |
| Calcium blocker | 250                    | 700 million                              |
| ACEI        | 1000                   | 2.8 billion                              |
| Antidiabetic |                        |                                          |
| Biguanide-Metformin | 200                    | 240 million                              |
| Insulin     | 350                    | 420 million                              |
| Renal replacement treatment |               |                                          |
| Peritoneal dialysis | 36,000                | ~1.4 billion*                            |
| Hemodialysis | 63,000                 | ~2.5 billion*                            |

* Projection was made from about 1% of patients with diabetes or hypertension developing ESRD
ACEI = angiotensin-converting enzyme inhibitors.
ESRD = end stage renal disease
Furthermore, and until now, in ordinary secondary care in Kinshasa, renal complications are assessed only by serum creatinine alone instead of resorting to formula-based estimates of creatinine clearance or eGFR. Consequently, many cases of CKD could be missed by using the serum creatinine alone.

In this present study, we found a discrepancy between prevalence of dipstick positive protein and proteinuria mainly in CKD stage 3. This difference may be due to the fact that only patients with dipstick positive protein 3+ were tested for 24-hour proteinuria. It also confirms differences in sensitivity and specificity between tests as reported recently by Konta et al. [27]. In their survey, the authors have demonstrated that dipstick positive proteins are more indicative of microalbuminuria than macroalbuminuria.

However, despite the fact that dipstick proteinuria has limited diagnostic value, it is of a great prognostic value. Indeed, dipstick positive protein has been associated with increased risk of cardiovascular events, including the development of HTN [28], DM [29], and ESRD [30]. But not all studies are in agreement [31] and it is unclear whether microalbuminuria is a marker of kidney disease or generalized vascular disease [32].

As expected [33], HTN, DM and proteinuria were independently associated with CKD 3+. Inadequate BP and/or poor glucose control may explain the CKD that we observed. The lack of BP control shown in our patients with HTN, of whom 78% were uncontrolled, is a bit higher than the 73% seen in Americans [34]. In addition, only 6% of participants with HTN and 4% of patients with DM and HTN having CKD had their BP controlled to the JNC VII recommended level of less than 130/80 mmHg [18]. This level of control is lower than the 20% in the New Opportunities for Early Renal Intervention by Computerised Assessment study (NEOERICA) [35] and the 11% reported in the National Health and Nutrition Examination Survey (NHANES III) [34]. It highlights the inadequate levels of BP control in this screening population, placing them at risk for cardiovascular and/or renal events, particularly ESRD [8] and may thereby increase medical care costs. Only 23% of all studied population received treatment to block the renin-angiotensin system. Certainly, ACEI may be less effective in Blacks, in whom the incidence of high renin hypertension is lower than in Caucasian population. However, the African-American Study of Kidney Disease and Hypertension (AASK) confirmed the reno-protective effects of ACEI compared to calcium blocker in Blacks with hypertensive nephropathy [36]. Also, in this AASK trial [36], an average of 2.6 drugs was needed to achieve BP goals, while the average number of drugs used by patients with HTN in the present survey was 1.3.

However, a secondary analysis of AASK study [37] comparing ACEI versus β blocker and Calcium blocker versus β blocker have shown that BP control does not always prevent progression of renal failure. These findings suggest that factors other than BP elevation likely participate in the progression of “hypertensive“ nephrosclerosis. But, we note that in this study [37], the authors did not test the hypothesis that treatment versus no treatment of HTN preserves kidney function. The bulk of evidence shows that BP control slows the progression of hypertensive kidney diseases, and control of the BP is not good in Kinshasa.

### Table 6: Risk factors associated with CKD.

| Determinants                              | OR (univariate analysis) | OR (multivariate analysis) |
|-------------------------------------------|--------------------------|----------------------------|
|                                           | CI 95% | P  | CI 95% | P  |
| CKD stage ≥ 3                             |        |    |        |    |
| HTN versus no                             | 2.9    | 1.9 – 4.6 | 0.001 | 3.3 | 1.7 – 6.5 | 0.001 |
| Pulse pressure > 60 versus < 60 mmHg      | 2.0    | 1.3 – 3.2 | 0.001 | 1.09 | 0.6 – 1.8 | 0.7  |
| Age ≥ 50 versus <50 years                 | 1.8    | 1.2 – 2.7 | 0.002 | 1.5 | 0.9–2.4 | 0.08  |
| DM versus no                              | 1.5    | 1.04–2.3 | 0.04   | 2.0 | 1.1–3.8 | 0.01  |
| Dipstick proteinuria ≥ 1+ versus 0        | 2.9    | 1.7–5.1 | < 0.0001 | 2.0 | 1.1–3.6 | 0.02  |
| Herbal remedy use versus no               | 1.7    | 1.03–2.7 | 0.002 | 1.2 | 0.7–1.9 | 0.3   |

24 h- quantitative proteinuria (≥ 300 mg/24 h)

| Determinants                              | OR (univariate analysis) | OR (multivariate analysis) |
|-------------------------------------------|--------------------------|----------------------------|
|                                           | CI 95% | P  | CI 95% | P  |
| Pulse pressure > 60 versus < 60 mmHg      | 2.4    | 1.5–3.9 | < 0.0001 | 1.8 | 1.03 – 3.2 | 0.03 |
| HTN versus no                             | 1.7    | 1.1–2.8 | 0.01   | 1.2 | 0.7 – 2.2 | 0.4   |
| DM versus no                              | 1.7    | 1.05–2.8 | 0.03   | 1.4 | 0.8–2.4 | 0.1   |

Abbreviations: CKD 3+ (eGFR < 60 ml/min/1.73 m²), CKD = chronic kidney disease, CI = confidence interval, DM = diabetes, HTN= hypertension.
HTN was also common with type 2 diabetes, which was more frequent than type 1 in the present study. In addition, most patients with DM in this study had poor glucose control. Appropriate management of DM and HTN are important to both the prevention and control of renal disease [23]. Awareness by patient and health care provider will help in this regard, and our study has advanced that awareness in Kinshasa.

Age and duration of DM also influenced the occurrence of CKD in this present study.

Duration of DM is well recognized as an important risk factor for diabetic nephropathy [9]. But duration of HTN did not have a correlation with low eGFR in this survey. That fits well with the fact that in most cases of renal diseases, HTN is the result of, rather than the cause of, the low eGFR. However, we do not know the exact causes of low eGFR in the subjects of this study.

CKD can also result from transmissible diseases such as HIV infection. Our observations show that the prevalence of CKD among HIV positive people is 12%. This value is lower than the 20% found in Uganda [38] and the 27% reported in Soweto [39]. It is on the other hand higher than the 2% [40] and 0.7% [41] described in the USA and in Ethiopia, respectively. This discrepancy of prevalence between these studies could be due to the difference in methodology applied in each survey. It could also reflect an ethnic disparity [42], or even a socio-economic gradient. But, it is hard to determine the true CKD prevalence among HIV population because a validated eGFR method does not exist in HIV subjects.

Among patients with a family history of kidney disease, the proportion of CKD was 8%. In addition, while Ramirez et al [43] showed that FH-KD was a strong determinant of proteinuria, with OR of 2.5, FH-KD in our survey was not associated with proteinuria or with reduction of kidney function. This observation may due to low awareness of CKD and its familial associations by both health workers and the lay population.

Another preventable risk factor for CKD is the use of herbal remedies, which was found in our study in univariate analysis but not in multivariate analysis. Others have reported renal toxicity and other adverse effects of traditional herbal remedies [44]. We can not state which of the remedies are nephrotoxic since studies of their composition are lacking.

Some risk factors for CKD such as smoking or LBW, reported elsewhere [43], were not observed in the present study. However, most of our study population did not have birth certificates or knowledge of their weight at birth, so the risk of LBW is probably not adequately assessed in this study. The reason why tobacco use was not associated with proteinuria remains unclear and deserves further attention.

An important issue that is not resolved by this study is how to reach high-risk individuals who do not attend these clinics as well the problem of payment for antihypertensive and antidiabetic drugs.

We think that our recent model of annual screening for proteinuria and CKD risk factors [45] combining educational message, detection and management of risk factor in general population may contribute partly to reach this first goal.

However, despite their benefits, treatments of HTN and/or DM are costly. This limits their use in SSA, where about half the population lives on less than $ 1 per day [3]. In Kinshasa the annual cost of drugs for optimal antihypertensives such as thiazide diuretics, calcium blocker, or ACE inhibitors, ranges from US $ 100, $ 250, and $ 1000 per patient, respectively, as estimated from a weighted average of wholesale prices for five proprietary products in the market. In this city, it is currently estimated that there are 2.8 million hypertensives [4]. Thus, if all hypertensives were treated with one or more of these drugs we can project that annual cost for these drugs would be between $ 280 million and $ 2.8 billion. If the same drugs are used in combination, the cost of the treatment would be even higher. In patients with DM, the estimated cost per patient of oral antidiabetics and insulin are about $ 200 and $ 350 per year, respectively. If we extrapolate these figures to the current 1.2 million diabetics in Kinshasa [4], the annual cost is over $ 240 million for biguanide-metformin and $ 420 million for insulin. The expenditure in patients with DM and HTN would be even higher. On the assumption that 1% of the hypertensive or diabetic population would evolve to ESRD there would be 28,000 hypertensives and 12,000 diabetics requiring RRT. Hence, we can project the annual cost for RRT in Kinshasa at ~$1.4 billion for peritoneal dialysis or ~2.5 billion for hemodialysis. These estimates for the cost of RRT will be higher if more hypertensives and/or diabetics progress to ESRD. It is clear that long-term dialysis will not be an option for most Africans with renal failure, and it is also likely that the use of anti-hypertensives and better treatment for DM will only reduce, not eliminate, the number of cases of diabetic and hypertensive nephropathy that evolve to ESRD. That said, the increased use of anti-hypertensives and better treatments for DM may reduce non-renal morbidity and mortality, which may make these treatments worth their expense. Indeed, El-Nahas [1] has made a case for the cost-effectiveness of screening for CKD, worldwide, in all populations.
We believe that use of anti-hypertensives and anti-diabetic treatment will reduce morbidity and mortality, but the magnitude of this benefit is not known. Still, in consideration of the combined cost of anti-hypertensive and diabetic treatment, as compared to the expense of cardiovascular disease and chronic dialysis, the cost of anti-hypertensive and diabetic treatment is cheaper. Thus, we need the support of the pharmaceutical industry as well as community support to supply developing countries with necessary renoprotective and cardioprotective drugs.

Furthermore, it is noteworthy that this study population has a very different age distribution from that of the DRC in general, the subjects of this study having an older age than that of the general population of Kinshasa. This could suggest that there will be an increasing number of such at-risk subjects in the near future. Hence, this situation is likely to worsen over the next 20 years if no effective preventive measures are taken.

All health care workers will need to be engaged in this effort. It is impossible that a few nephrologists would be able to implement detection and prevention of CKD for the whole city, let alone the entire DRC. Indeed, in 2004, the DRC counted only 0.11 physicians per 1000 population and 0.52 nurses per 1000 population [46]. Consequently, management of the patients in this country must be by nurses for primary care and by general practitioners for secondary care. Adapting K/DOQI guidelines must account for local conditions and manpower.

**Strength and limitation of our study**

The strength of our survey is that it includes patients at-risk for CKD follow-up in multiple centres of primary as well as secondary health care and that we used a random sample and standardised methods of data collection. Already, by doing this study, we have improved awareness of optimal CKD care in traditional health care system of Kinshasa.

Our study has certain limitations. It is a cross-sectional snapshot analysis with 24-hour urinary protein not measured in every patient and serum creatinine measured only once. This may overestimate CKD. It has also a relatively small size, and it relies on the MDRD equation, the validation of which is lacking among African populations as well as in those with HIV. Moreover, the inaccuracy of 24 h urine collection may also over or underestimate CKD. Finally, although all participants were chosen randomly by the local team, it is possible that the choice was made among the more affected patients having needed specialized opinion.

**Conclusion**

Despite the above limitations, our findings show the effectiveness of community based targeted health screening program, in identifying significant numbers of persons with CKD previously undiagnosed, and also in finding those with inadequate risk-factor control. This study suggests that there is a great potential for decreasing CKD as well as ESRD incidence and cardiovascular morbidity or mortality by optimizing modifiable risk factors in this high-risk population. It also suggests that the costs of treating those with CKD may be cost-beneficial, by averting the morbidity of cardiovascular disease and also the very high cost of RRT. Furthermore, our study emphasizes the urgent need for increased training of generalist physicians and nurses in CKD prevention programs as well an active collaboration between traditional health care and nephrology services.

The establishment of prevention programs in developing countries is also a political and financial challenge. This challenge could be taken up by creation of international funding assistance as exists for HIV or tuberculosis infection, the goal of which would be to support the program of prevention of CKD, and some of its risk factors such as HTN, DM and obesity.

Finally, further study is needed to improve the precision of these preliminary data and to assess the benefit of anti-hypertensive such as ACEI on the progression of renal disease in Black Africans. That is because studies in Afro-Americans may probably not be directly applicable to Sub-Saharan Africans and extrapolation must be made with caution.

**Competing interests**

The authors declare that they have no competing interests.

**Authors' contributions**

EKS designed the study, acquired data, analyzed, interpreted data, drafted and revised the manuscript. EPC interpreted data, drafted and revised the manuscript. CVZ acquired data and revised the manuscript. JMK interpreted data, drafted and revised the manuscript. NMN interpreted data and revised the manuscript. All authors read and approved the final manuscript.

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