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Factors Associated with Chronic Kidney Disease in Patients Living with HIV in Yamoussoukro (Ivory Coast)

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Abstract

Introduction: Human immunodeficiency virus (HIV) infection is an epidemic in sub-Saharan Africa and is a risk factor for kidney disease. The aim of this study was to assess the prevalence of chronic kidney disease (CKD) in patients living with HIV (PLHIV) in Yamoussoukro and to identify associated factors. Methods: This was a cross-sectional analytical study conducted at the Walè Medical and Social Centre in Yamoussoukro from 4 January to 31 July 2021. The study involved people living with HIV, aged at least 18 years, on Highly active antiretroviral therapy (HAART) protocol, without glomerular filtration rate (GFR) or urine sediment abnormalities, with a complete medical record and having given informed consent. CKD was defined as GFR < 60 ml/min/1.73m^2, and/or albuminuria ≥ 30 mg/gCr observed on two assays spaced at least 3 months apart. Data were analysed using Epi-Info software. Results: Of the 174 PLHIV included, 46 were men and 128 were women, giving a sex ratio of 0.4. The mean age was 46.5 years (extremes 19 and 74 years). The majority (96.6%) were infected with HIV-1. The patients were at stage B2 in 36.2% of cases and the mean CD 4 count was 622 cells/ mm3. The first-line treatment regimen included tenofovir disoproxil fumarate (TDF) in 94.3% (164/174). At inclusion, 15 patients (8.6%) had a GFR < 60 ml/min and 52 patients (29.9%) had an ACR) ≥ 30 mg/gCr. At month 3 control, 11 patients (6.3%) had a GFR < 60 ml/min, and 52 (29.9%) had an ACR ≥ 30 mg/gCr. CKD was present in 46 (26.4%) cases. The occurrence of CKD was associated with the presence of high blood pressure (P = 0.014) and would be associated with the use of tenofovir -based therapeutic protocols (P = 0.004). Conclusion: CKD is relatively common in people living with HIV.

Early detection is essential in the follow-up of infected patients. We recommend that all PLHIV on HAART be screened for renal abnormalities by measuring blood pressure and creatinine levels, estimating GFR, looking for proteinuria and careful choice of antiretrovirals, and proactive management of comorbidities.

Keywords

HIV, Chronic Kidney Disease, Screening, Tenofovir

1. Introduction

HIV, an infectious viral disease, is a major public health problem worldwide. In 2022, an estimated 39.0 million people [33.1 to 45.7 million] were living with HIV, and 630,000 people [480,000 to 880,000] died of HIV-related causes. Africa is the region most affected, with three-quarters of all PLHIV) [1] [2]. Ivory Coast is one of the most affected countries in the West African sub-region, with a 2020 prevalence of 2.3% and an estimated incidence of 0.24 per thousand [2]. The country recorded 12,000 deaths in 2020 [2] [3]. Combination antiretroviral therapy (ART) has transformed the bleak vital prognosis of infected subjects. Life expectancy for PLHIV has now been extended, and complications such as kidney, liver and heart disease have largely replaced opportunistic infections as the main causes of death in the context of HIV [4]. The HIV-infected patient is at risk of kidney disease through multiple mechanisms: either through direct viral damage to anatomical structures or the risk of nephrotoxicity due to antiretroviral treatment, or other co-morbidities of infected subjects. The worldwide prevalence of chronic kidney disease among PLHIV is estimated at 6.4% [5]. Recent epidemiological studies confirm the high frequency of kidney disease in Africa, ranging from 15.5% to 38% [6]. In Ivory Coast, earlier studies in Abidjan showed an estimated 24% prevalence of CKD in untreated PLHIV [7]. In the era of the 95% screened and treated strategy, we initiated this study to assess the prevalence and determine the associated factors of chronic kidney disease (CKD) in HIV-positive subjects followed up in Yamoussoukro, with a view to improving prognosis.

2. Patients and Methods

We conducted a cross-sectional, prospective, analytic study at the Walè medico-social center in Yamoussoukro from January 4 to July 31, 2021.

The study population consisted of HIV-infected subjects followed up at this first-contact health center. All patients at least 18 years of age, living with HIV, on HAART protocol, with no abnormalities in glomerular filtration rate (GFR) or urine sediment, with a complete medical history and having given voluntary informed consent, were included in the study.

Patients with heart failure, fever, and urinary tract infection during the survey or treated for chronic kidney disease were not included in the study. The survey was conducted in 2 stages (initiation at month 0 and control at month 3) spaced

at least 3 months apart.

At the first visit to the month 0 (M0), the doctor in charge of the survey sat the patient down and labeled the urine jars with the patient's name. He explained to the patient how to collect the urine in the labelled jars. The doctor ensured that the urine jars were correctly labelled with the patient's ID and handed them back to the patient, together with the urine tracking sheet. An initial dipstick test was performed to check for urinary tract infection or hematuria. If the test was negative, the doctor called the patient for an appointment within 48 hours of the date of signing the consent form. At the 48-hour appointment, urine tests and blood samples were taken.

Urine was examined for albuminuria and the albuminuria-to-creatinuria ratio using the semi-automatic UC-1000 SYSMEX® analyzer. The UC-1000 SYSMEX® analyzer is a semi-automatic urinary chemistry device for systematic analysis of the patient's urine. Blood sampling was carried out in the morning in subjects fasting for 12 hours, by venipuncture at the elbow into a dry red tube (without anticoagulant), using sterile, single-use equipment.

At month 3 (M3), the doctor took care to call the patient the day before to remind him of the appointment, and the process was identical to that in month 0 (M0). A standardized survey form was used to collect socio-demographic, clinical, para-clinical and therapeutic parameters (**Appendix**). In the present study, CKD was defined as a decrease in GFR below 60 ml/min/m^2 and/ or albuminuria (A/C > 30 mg/gCr) observed on 2 determinations spaced at least 3 months apart. Glomerular filtration rate (GFR) was estimated using the (Modification of diet in renal disease) MDRD formula. Albuminuria was considered normal when values were < 30 mg/24 hours. Microalbuminuria was defined as a urinary albumin level between 30 and 299 mg/24 hrs, and macroalbuminuria as an atux greater than 300 mg/24 hrs.

BMI was calculated using the formula: BMI = weight kg/height m^2. Patient weight was measured on a 150 kg mechanical scale with an accuracy of 0. 1kg. Patient height was measured using a wall-mounted height gauge with a precision of 0.1 cm. Patients with a BMI between 12.5 and 16 kg/m^2 were considered malnourished. Those with a BMI between 16.5 and 18.5 kg/m^2 were considered lean, those with a BMI between 25 and 30 kg/m^2 were considered overweight, and those with a BMI greater than 30 kg/m^2 were considered obese. Data analysis was performed using SPSS 21.0 software. Quantitative variables were expressed as mean with standard deviation and extreme values. Qualitative variables were expressed as proportions.

Proportions were compared using the Fisher, Yates, CHI-2 tests at the $\alpha = 5\%$ threshold. This study was carried with good clinical practice and national and international medical research guidelines. An authorization was sent to the regional health department and to the medical and scientific director of the aforementioned center. The confidentiality of the data collected was scrupulously respected.

3. Results

Out of a total of 300 patients selected, 96 were absent, i.e. 204 at initiation (M0)

and at month 3 (M3), 174 responded to the invitation, i.e. a response rate of 85%. The study population consisted of 174 PLHIV, 46 men and 128 women, i.e. a sex ratio of 0.4. The mean age of the patients was 46.5 ± 12.5, with extremes of 19 and 74 years. The 40 - 60 age group was the most represented, with 107 (61.5%) cases. More than two-thirds of patients (82.8%) lived in urban areas.

In terms of educational level, 61 (35. 0%) cases were illiterate. 110 (63.2%) patients worked in the informal sector. 59 (33.9%) were living common-law. The proportion of HIV 1 cases in our cohort was 168 (96.5%). Patients reported taking traditional medicines in 90 (51.7%) cases, and non-steroidal anti-inflammatory drugs in 31 (17.8%) cases. One hundred and eleven patients (63.8%) had been on ARVs for at least 5 years, with a median of 7 years.

In terms of clinical signs, at M0 body mass index (BMI) revealed obesity in 23 (3.2%) cases. At M3, obesity was observed in 40 (14.4%) patients. Blood pressure was normal in 139 (79.9%) cases at M0, and in 151 (86. 8%) cases at M3. Clinical classification according to CDC showed stages B2, A1 and C1 in 36. 2%, 20.1% and 13.2% of cases respectively (Table 1).

Table 1. Distribution of socio-demographic characteristics according to the occurrence of CKD.

Parameters	CKD		P-value
	Positive	Negative	
Age			
<40 years old	10 (5.8%)	37 (21.3%)	0.948
[40 - 60 years old]	29 (16.7%)	78 (44.8%)	0.801
>60 years old	7 (4.0%)	13 (7.5%)	0.356
Gender			
Female	38 (21.9%)	90 (51.7%)	0.105
Male	8 (4.6%)	38 (21.8%)	
Area of residence			
Urban	23 (13.2%)	105 (60.3%)	0.672
Rural	7 (4.0%)	23 (13.2%)	
Marital status			
Married	13 (7.6%)	29 (16.7%)	0.446
Single	12 (6.9%)	38 (21.8%)	0.643

At M0, the mean CD4 count was 622 elements/mm^3 and 677 elements/mm^3 at M3. Nine patients (5.2%) and 7 patients (4.0%) had CD4 counts <200 elements/mm at M0 and M3 respectively. Patients with a normal CD 4 count ≥ 500

cells/mm^3 were the most represented at 62.1% and 72.4% respectively. The mean viral load was 4.4 cp/ml at both M0 and M3. Mean hemoglobin was 12.4 g/dl at M0 and 11.8 g/dl at M3. Mean creatinine was 12.4 g/dl at M0 and 9.3 mg/l at M3. Mean GFR was 70.7 ml/min/1.73m^2 at M0 and 99.3 ml/min/1.73m^2 at M3. Fifteen patients (8.6%) had a GFR < 60ml/min at initiation, and at M3 there were 11 (6.3%). At M0, 23 (13.2%) patients had positive urine dipstick proteinuria. In terms of albuminuria to creatinuria ratio, microalbuminuria was present in 47 (27.0%) cases and macroalbuminuria in 5 (2.9%). At M3 at the urine dipstick, proteinuria was positive in 66 (37.9%) cases. In terms of albuminuria to creatinuria ratio, microalbuminuria was present in 52 (27. 9%) cases and macroalbuminuria in 4 (2.1%) cases.

Forty-six subjects had developed chronic kidney disease (26.4%). Ninety-eight percent of patients were on first-line ARV therapy. At M0 and M3, the ARV regimens were Tenofovir (TDF)-Lamivudine (3 TC)-Efavirenz (EFV) in 82 (47.1%) cases and TDF-3TC-Dolutegravir (DTG) in 80 (46. 0%) cases. Patients were on cotrimoxazole prophylaxis at M0 in 34. 5% and at M3 in 20. 1% of cases (Table II). The occurrence of CKD was related to the presence of hypertension (P = 0. 000) and to the use of TDF in treatment regimens (P = 0.004) (Table 2).

Table 2. Distribution of clinical, biological and therapeutic characteristics according to the occurrence of CKD.

Parameters	CKD		P-value
	Positive	Negative	
Comorbidities			
High blood pressure	17 (8.1%)	14 (9.8%)	**0.000**
Diabetes	4 (2.3%)	5 (2.9%)	0.208
Obesity	11 (6.3%)	29 (16.7%)	0.86
BMI			
Low weight	7 (4.0%)	20 (11.5%)	0.948
Normal weight	29 (16.7%)	70 (40.2%)	0.326
Overweight	5 (2.9%)	20 (11.5%)	0.43
Obesity	5 (2.9%)	18 (10.%)	0.583
Type of VIH			
HIV 1	43 (24.7%)	125 (71.8%)	0.183
Duration of HIV treatment			
5 years	13 (7.5%)	11 (28.7%)	0.515
[5 - 10 years]	19 (10.9%)	43 (24.7%)	0.075
>10 years	14 (8.1%)	35 (20.1%)	**0.0349**

Continued

Previous therapeutic protocol			
TDF	39 (22.4%)	124 (71.6%)	**0.004**
Cotrimozaxole	19 (10.9%)	50 (28.7%)	0.79
High blood pressure			**0.014**
M0	15 (8.6%)	20 (11.5%)	
M 3	11 (6.3%)	12 (6.9%)	
Anemia			0.052
M0	31 (17.8%)	65 (37.4%)	
M3	32 (18.4%)	74 (42.5%)	
Therapeutic line			
First line	44 (27.3%)	127 (73.0%)	0.111
TDF (M0)	39 (22.4%)	124 (71.3%)	**0.004**
TDF (M3)	39 (22.4%)	124 (71.3%)	
Cotrimoxazole (M0)	13 (7.5%)	47 (27.0%)	0.31
Cotrimoxazole (M3)	7 (4.0%)	28 (16.1%)	
NSAID (M0)	2 (1.2%)	2 (1.2%)	0.28
NSAID (M3)	1 (0.6%)	0 (00%)	

BMI: body mass index, NSAID: non-steroidal anti-inflammatory drug.

4. Discussion

Kidney damage in HIV is on the increase in a population already weakened by HIV. A study on this subject is of the utmost importance, given the poor data available in sub-Saharan Africa, and especially in Ivory Coast. The aim of this study was to assess the prevalence of CKD in PLHIV on HAART in Yamoussoukro, and to identify associated factors.

One of the limitations of this work was the refusal of some patients to participate. Indeed, living with HIV often requires frequent medical visits, tests and regular monitoring of many aspects of health, including kidney function. Patients may feel psychological and physical tiredness at the additional medical burden of participating in a survey. In addition, the clinical and biological data recorded in the medical records were incomplete for some patients, limiting the size of our sample. Unfavorable socio-economic conditions meant that some patients were unable to attend M3, resulting in many patients being lost to follow-up.

In this study, the mean age of patients was 46.5 ± 12.5 years. These results are comparable to those reported by Morquin and colleagues [8] in France, where the mean age was 43 years, but lower than those reported by Gizachew and colleagues [9] in Ethiopia, who found a median age of 39.7 (±9.7) years. The female

predominance of our patients is corroborated by several studies [5] [8]. According to The Joint United Nations Programme on HIV/AIDS (UNAIDS) [2] data for sub-Saharan Africa, six out of seven new infections among adolescents are among girls. The biological vulnerability of women to HIV infection may be explained by the anatomo-histological differences between men and women at genital level. The risk of transmission is about twice as high from man to woman as from woman to man during heterosexual intercourse. This is because the female genital tract has a greater surface area of mucous membrane exposed to sexual secretions and microtrauma, and semen contains a higher concentration of virus than vaginal secretions [10].

The majority of our patients had HIV 1 infection (96.6%). Guei and colleagues [7] found a predominance of HIV 1 at 97.2%. This finding is in line with all the literature and several specialized organizations, including UNAIDS, which indicate that HIV 1 is the most prevalent type worldwide [2]. With regard to comorbidities, 17.8% of participants had high blood pressure. This result was higher than that of Taklo and colleagues [11], who found a prevalence of 6.4%. This could be explained by the fact that the age group most represented in our cohort was 40 and over, and that cardiovascular disease can occur at this age.

There was a significant association between the presence of high blood pressure and CKD (P = 0.000). High blood pressure is both a cause and often a consequence of CKD. High blood pressure, one of the main causes of chronic kidney disease, damages the small blood vessels that drain blood to the kidney filters. Long-term, untreated hypertension will lead to reduced blood flow to the kidney filters, and can result in chronic kidney failure. Patients with clinical stage B2 according to the CDC classification were the most numerous (36.2%). In other studies, such as that by Taklo and colleagues [11] in Ethiopian, the World Health Organization classification was used, and 66.7% of patients were in stage 2. These different stages correspond to the risk of minor HIV-related opportunistic infections. Micro- and macro-albuminuria were observed in 27.6% of patients at initiation and 2.3% at the third month. Msango and colleagues [12] in Tanzania made a similar finding in their series, with microalbuminuria at 28.8% in a population of HIV-infected children, and Han and colleagues [13] in South Africa found 24%. On the other hand, Collen and colleagues [14] in the United States of America found lower results at 14.0%. Albuminuria, and even better the urine albumin/creatinine ratio, is a prognostic marker whose increase precedes GFR decline. Overall, differences in screening methodologies, clinical characteristics and associated comorbidities of study participants could explain the diverse results compared to those of our study.

Among ARV regimens, 94.3% contained TDF. This percentage as similar to that of Guei and colleagues [7]. In our study, the use of TDF in different ARV regimens was statistically associated with the occurrence of CKD (P = 0.004). Among the antiretrovirals that can potentially increase the risk of kidney damage, TDF is one of the drugs commonly used in antiretroviral therapy that has a higher

risk of developing chronic kidney disease [15]. Tenofovir is excreted in the urine by proximal tubular epithelial cells. In the event of cytoplasmic accumulation, tenofovir inhibits mitochondrial deosyribonucleic acid polymerase γ, resulting in respiratory chain dysfunction and, in turn, energy-deprived cell damage. Fanconi syndrome is the clinical expression of acute tenofovir toxicity, sometimes associated with acute renal failure [15]. Patients treated with TDF are at increased risk of proteinuria, reduced GFR and chronic renal failure [16].

5. Conclusion

CKD is common in PLHIV. Early detection is essential in the follow-up of infected patients. We recommend that all PLHIV on HAART be screened for renal abnormalities by measuring blood pressure and creatinine levels, estimating GFR and checking for proteinuria.

Authors' Contributions

- Koffi Christ Ziahy Reine-Marie: drafting of the manuscript, bibliographical research.
- Yao Sébastienne: data collection, development of the survey form.
- Gnohité Grâce: data collection.
- Kpan Kéhi Jonathan: development of the survey form.
- Gonan Abdoul Yanick: bibliographical research.
- Affi Mélèdje Césaire: study initiation, data collection.
- Wognin Manzan, data collection.
- Tia Weu Mélanie: study initiation, data collection, manuscript correction.
- Ouattara Bourhaïma, manuscript correction.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

Survey Form

1) Anthropometric data

First and last name: _____

Age: _____

Sex: ☐ Male ☐ Female

Area of residence: ☐ urban ☐ rural

Date of HIV diagnosis: _____

Marital status: ☐ Single ☐ Married

Level of education: ☐ None ☐ Primary ☐ Secondary ☐ Higher

Current employment: ☐ Yes ☐ No

2) Medical history Previous

kidney disease: ☐ Yes ☐ No

If yes, specify nature and duration of disease: _____

Hypertension: ☐ Yes ☐ No Diabetes: ☐ Yes ☐ No

Other comorbidities: ☐Hepatitis B ☐ Hepatitis C ☐ Other (specify): _____

List of medications currently taken (other than antiretrovirals):_____

date of discovery (HIV):……..

ARV treatment: _____ine: _____

Total duration of antiretroviral treatment : _____ years

Impact on quality of life (self-assessment): ……

General state of health: ☐ Very good ☐ Good ☐ Fair ☐ Poor

CDC clinical stage: ☐ A ☐ B ☐ C

Cotrimoxazole prophylaxis over the last 6 months: ☐ yes ☐ no

Traditherapy ☐ oui ☐non

Smoking: ☐ Yes ☐ No ☐ Former smoker

Alcohol consumption: ☐ Yes ☐ No ☐ Occasional

3) Clinical data

Weight M0	Weight M3
Height M0	Height M3
BMI M0	BMI M3
BP M0	BP M3
Heart rate M0	Heart rate M3
Proteinuria M0	Proteinuria M3
Hematuria M0	Hematuria M3
Leukocyturia M0	Leukocyturia M3
A/C M0	A/C M3

4) Biological data

Creatinine M0	Creatinine M3
GFR M0	GFR M3
CD4 count M0	CD4 count M3
Viral load M0	Viral load M3