



Kidney Disease and HIV Infection: Epidemiological and Clinical Aspects in N'Zérékoré Regional Hospital (Guinea)

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Abstract

HIV infection can affect all organs and renal involvement is common. The prevalence of renal abnormalities has been estimated at approximately 30% of patients. **Patients and Methods:** This was a prospective cross-sectional descriptive study over a period of six (6) months from April 30, 2017 to October 30, 2017. **Results:** During our study, 147 HIV-infected patients were registered in the medical department of the Regional Hospital of N'Zérékoré, among which 62% or 42.18% met our criteria and presented kidney disease. The age group of 46 - 55 years was the most represented with a frequency of 48.39%. The average age was 40 ± 6.32 years with extremes of 18 and 62 years. Almost all of our patients had polymorphic clinical manifestations dominated by physical asthenia with 91.94%, followed by fever with 83.87%, headache with 80.65% and diarrhea with 80.65%. The most represented physical sign was the pallor of the tegument and conjunctive with 56.45%, the oedema of the lower limbs with 43.55%. The markers of renal damage in our patients were dominated by proteinuria with 69.35%. Of the 62 patients with kidney disease, 47% or 75.80% were placed in the context of organic kidney damage and the types of damage most represented during our study were glomerular damage with 43.55%, followed by tubule-interstitial damage 22.58%. Chronic renal failure was the most observed type of failure in our patients with 60% against 40% of cases of acute renal failure. **Conclusion:** Kidney disease is very common and varies during HIV infection. Screening for kidney disease in the HIV population is therefore fundamental because its early diagnosis should allow the identification of patients at high risk of progression of kidney disease but also of hospitalization and mortality.

Subject Areas

HIV, Nephrology

Keywords

Kidney Disease, HIV, HIVAN

1. Introduction

Human immunodeficiency virus (HIV) infection is a major cause of morbidity and mortality worldwide. HIV has become a chronic disease in countries where patients have access to combination antiretroviral therapy. The infection is present in all continents, but two-thirds of the infected population live in sub-Saharan Africa. The infection can affect all organs and renal involvement is common. The prevalence of renal abnormalities has been estimated at approximately 30% of patients [1]. The prevalence of chronic renal failure is estimated at 5% [2]. HIV related nephropathy (HIV) is the main glomerulopathy induced directly by HIV. HIVAN was the most frequent nephropathy discovered on kidney biopsy of population living with HIV (PLHIV) until the era of highly effective ARV treatments. The incidence of ARI remains high at around 5% to 20% [3]. Risk factors for ARI are advanced immunosuppression, high viral load, hypovolemia and infections.

In a cross-sectional study carried out in Malawi on 526 antiretroviral treatment-naïve patients who were at WHO stages 1 and 2, 63.8% had a CD4 count < 350 cells/mm³ and the prevalence of renal failure was 10.6% [4]. In a study of black patients with chronic renal failure at the University Hospital of Treichville in Abidjan, nephropathy associated with HIV infection was 17% of cases. Almost all of the patients (97.3%) consulted when faced with polymorphic clinical manifestations [5].

In Guinea in 2016, M L Kaba, *et al.* reported a prevalence of 24% renal failure in HIV-infected patients with a male predominance of 73% [6]. Our objectives were to determine the frequency of kidney disease in HIV-infected patients in the general medicine department of the Regional Hospital of N'Zérékoré (GUINEA).

2. Patients and Methods

This was a prospective study conducted from April 30, 2017 to October 30, 2017. We targeted all HIV patients with kidney damage admitted to the general medicine department. We included all HIV+ patients whose age is greater than or equal to 15 years, in whom a marker of renal damage was detected on the urinary dipstick and/or a serum creatinine. Our variables were epidemiological (the prevalence reflected as a percentage is the ratio of patients with renal impairment with HIV+ status to the total number of patients with HIV+ status admitted to the department during the study period, age, clinical variables were represented by the risk factors for chronic kidney disease including advanced age greater than or equal to 60 years; A low CD4 count of less than 200

cells/mm³; taking nephrotoxic substances: decoctions, anti-inflammatories, susceptible, ARVs mainly Tenofovir, hypertension, diabetes, hepatitis B was checked.

The symptoms sought were (general and/or functional): fever, physical asthenia, anorexia, weight loss, dyspnea; pruritus, oligo-anuria, muscle cramps, polyuria, foamy urine, urinary burning, susceptible, nausea, vomiting, lumbar and abdominal pain, dysuria. We retained: the pallor of the integuments and conjunctiva, OMI/puffiness of the face, ascites; pleural effusion, heart rhythm disorder, low blood pressure. Markers of renal damage were detected or sought from the urine dipstick. We considered glomerular involvement in the presence of proteinuria \geq +++ (3 g/24 h) with or without hematuria, associated with hypertension. Tubulo-interstitial involvement with proteinuria \leq ++ (1 g/24 h) associated with aseptic leukocyturia. Vascular involvement with proteinuria \leq + (0.3 g/24 h) with or without haematuria, associated with hypertension, with left ventricular hypertrophy, stage III or IV hypertensive retinopathy on fundus examination. An ARF in the face of any rise in the plasma level of urea greater than 8.3 mmol/L and creatinine greater than 115 μ mol/L with normalization of the values at the second dosage 3 months apart (functional or organic). Chronic renal failure in the face of any persistence of markers of renal damage on the BU and/or a decrease in GFR $<$ 60 ml/min at the second dosage after 3 months apart and classified into five stages of increasing severity according to the GFR and/or the signs of chronic kidney disease including normochromic normocytic anemia are generative with a hemoglobin level below 12 g/dl. Hypocalcemia $<$ 2.2 mmol/L). The evolutionary character was repartitioned in favor by the improvement; and presented by death or complications (acute pulmonary oedema, heart attack, coma) or others by discharge against medical advice. We retained two (2) modalities: HIV1, HIV2; CD4 counts were divided into 3 classes below 350 cells/ml, 350 - 500 cells/ml and above 500 cells/ml and four clinical stages defined by the WHO, namely: stage 1, stage 2, stage 3 and stage 4 were retained. The data collection procedure was exhaustive and the data were recorded and analyzed by Epi Info 7.4.1 software. The information obtained was used in a purely scientific but confidentiality was in principle. The absence of the biopsy for the diagnostic confirmation, the realization of genetic test for the affirmation or the confirmation of the associated character of the kidney disease, HIV and APOL1. The financial difficulty of carrying out certain paraclinical examinations, in particular the complete ionogram, the NFS and the renal ultrasound, the absence of the biopsy for the diagnostic confirmation and the evaluation of the prognosis, the realization of genetic test for the affirmation or confirmation of the associated nature of kidney disease, HIV and APOL1, the delay in consulting patients were our main limitations and difficulties.

3. Results

During our study, 147 patients infected with HIV were registered in the general medicine department of the Regional Hospital of N'Zérékoré, among whom 62 or 42.18% met our criteria and presented with kidney disease. The age group of

46 - 55 years was the most represented with a frequency of 48.39%. The average age of our patients was 40 ± 6.32 years with extremes of 18 and 62 years. In our study, we noted a female predominance of 35 cases or 56% against 27 cases in men or 44%. The sex ratio was 0.7%. The potential risk factors for kidney disease were largely dominated by taking nephrotoxic substances with 83.87%.

Almost all of our patients consulted for polymorphic clinical manifestations dominated by physical asthenia with 91.94%, followed by fever with 83.87%, headaches with 80.65% and diarrhea with 80.65%. The most represented physical signs were the pallor of the teguments and conjunctiva with 56.45%, the edema of the lower limbs with 43.55%. The markers of renal damage in our patients were mainly dominated by proteinuria with 69.35%.

Of the 62 patients with kidney disease, 47% or 75.80% were placed in the context of organic kidney damage and the types of damage most represented during our study were glomerular damage with 43.55%, followed by tubulo-interstitial lesion 22.58% (**Table 1**).

According to the clinical context and the biological results, chronic renal failure was the most observed type of failure in our patients with 60% against 40% of cases of acute renal failure. The signs of chronicity were predominantly represented by anemia with 59.46% (**Table 2**).

The clinical evolution was favorable in 44 cases during our study period.

On the other hand, we recorded 9 cases of complications or 14.52%; 5 cases of death or 8.06%; 4 cases of discharge against medical advice, *i.e.* 6.45%. One hundred percent of our patients had positive HIV1 serology. The CD4 count was very low in most of our patients; 59.68% had a CD4 count $< 350/\text{mm}^3$. Thirty-three of our patients, or 53.23%, were classified as stage III (WHO) of HIV infection.

4. Discussion

We carried out a descriptive study in the general medicine department of the Regional Hospital of N'Zérékoré (GUINEA). The objective was to determine the prevalence and clinical manifestations of kidney disease in HIV-infected patients. We were faced with difficulties, such as the absence of kidney biopsy, the lack of genetic tests in the country. During our study, 147 HIV-infected patients were recorded, of whom 62% or 42.18% met our criteria and presented with kidney disease. We noted considerable presence of the risk factors of renal attack within our population in particular the frequency of the infection with HIV, the low rate of CD4, the abusive use of the potentially nephrotoxic substances (NSAIDs, traditional products), low socioeconomic status. Our result is much higher than that found by M. Cissé, *et al.* [7] in 2015 in Dakar who reported an average prevalence of 12.9% kidney damage. The average age of our patients was 40 ± 6.32 years. HIV infection has become an infection of the juvenile layer of chronic evolution. Similar results have already been reported by other authors. This is the case of Nyimi M.L. and Coll [8] in the DRC who reported an average age of 40.3 ± 9.6 years.

Table 1. Type of kidney disease.

Initial Nephropathy	Number	Pourcentage (%)
Glomela Nephropathy	27	43.55
Tubular Nephropathy	14	22.58
Vascular Nephropathy	06	9.68
Pre-Renal Disease	15	24.19
Total	62	100

Table 2. Type of renal failure.

Stade	Number	Pourcentage (%)
Stade I	3	8.11
Stade II	3	8.11
Stade III	21	56.76
Stade IV	8	21.62
Stade V	2	5.41

M.L. Kaba, *et al.* [6] in 2016 in Guinea in a study on the prevalence of acute and chronic renal failure in HIV-infected patients in Conakry reported an average age of 41 years. We noted a female predominance of 35 cases or 56% against 27 cases among men or 44%. The M/F sex ratio was 0.7%. The lack of awareness campaign, the low level of education and the use of self-medication are among factors that show a high prevalence in the young population. The potential risk factors for kidney disease were largely dominated by taking nephrotoxic substances with 83.87%. Indeed, we did not find studies reporting with precision the frequencies of the risk factors potentially involved in the onset of disease in PLHIV, but many studies cite as factors frequently involved, black race, low CD4 count, elevated viral load, co-infection with the hepatitis C virus, the existence of arterial hypertension and diabetes, patients with a longer cumulative exposure to tenofovir disoproxil fumarate, the expression of APOL1 which is an innate immunity gene. Some of these factors were found in our study at varying frequencies [9] [10] [11] [12] [13].

Almost all of our patients consulted for polymorphic clinical manifestations dominated by physical asthenia with 91.94%, followed by fever with 83.87%, headaches with 80.65% and diarrhea with 80.65%. These results would be linked to the fact that HIV infection is a pathology causing throughout its evolution physical asthenia, prolonged fever and diarrhoea.

The markers of renal damage in our patients were mainly dominated by proteinuria with 69.35%. The results are varied in the studies M. Cissé, *et al.* [7] in 2015 in Dakar in their study reported on 32 patients with renal impairment, 56% of cases having presented proteinuria with an average of 3.3 g/24 h. Microalbuminuria, a key sign of kidney disease but also a manifestation of metabolic syndrome and vascular dysfunction, is present in 10% - 15% of HIV-infected pa-

tients [14].

These results corroborate with data from the literature [15]. In the kidneys, it has been shown that HIV RNA can be localized to podocytes and to tubular cell epithelia, which explains the striking abnormalities seen in nephropathy. The HIV regulatory protein Nef and the HIV accessory protein Vpr, when overexpressed in mice, reproduces the nephropathy syndrome, suggesting that these proteins play a pathogenic role in HIV-associated nephropathy [16].

Of the 62 patients with kidney disease, 47% or 75.80% were placed in the context of organic kidney damage and the most represented types of damage were glomerular with 43.55%, followed by tubulo-interstitial damage 22.58%.

M. Cissé, *et al.* [7] in 2015 in Dakar in their study reported on 20 patients, 12 cases of glomerular involvement; tubulointerstitial and vascular lesions were present in 45% and 12.5% of cases, respectively.

These results could also corroborate with data from the literature which stipulate that viral replication leads, at the level of renal tissue, to the proliferation of glomerular and tubular epithelial cells, which is responsible for the lesions of these structures concerned [15] [17]. Although it is difficult in the clinical setting to determine whether glomerular disease is intrinsically linked to viral infection, clinical and experimental evidence exists to confirm the relationship between specific circulating immunoreagents associated with HIV, including idiotypic antibodies and antibodies against gp120, gp41 and p24, with the development of glomerulonephritis [18] [19] [20]. Co-infection with other pathogens, such as hepatitis C virus, may influence the pathogenesis of immune-mediated kidney disease by HIV causing inflammatory cell infiltration, leading to tubulo kidney disease—interstitials. According to the clinical context and the biological results, chronic renal failure was the most observed type of failure in our patients with 60% against 40% of cases of acute renal failure.

On the other hand, M.L. Kaba, *et al.* [6] in 2016 in Guinea in their study of 314 cases of kidney failure diagnosed in PLHIV; 69% (216 cases) of IRA were reported against 31% (98 cases) of IRC. Our result could on the one hand conform to data from the literature which shows that in the black race, HIV-related nephropathy (NVIH) represents the most common renal impairment, marked by a progressive evolution towards end-stage renal failure. And on the other hand it would be justified by the delay in the consultations of our patients. In Africa, any chronic disease is considered mystical. The patient therefore consults the hospital only after several unsuccessful detours to traditional healers. According to the DFG/MDRD, 56.10% of our patients were classified as stage III chronic kidney disease. Our result could be related to the high frequency of CKD found in our patients. The stigmata of chronicity were predominantly represented by anemia with 59.46%. This could be linked to the association of several mechanisms that are sources of anemia observable in PLHIV with renal impairment: malnutrition, frequent chronic opportunistic infections, the direct action of HIV on the hematopoietic system, the alteration of the synthesis of erythropoietin in renal impairment.

The clinical evolution was favorable in 44 cases. This favorable result is the willingness shown by doctors for the treatment of patients without forgetting the role of counselling. On the other hand, we recorded 9 cases of complications or 14.52%; 5 cases of death or 8.06%; 4 cases of discharge against medical advice, *i.e.* 6.45%. Patients linger with their pathologies and often show a great delay in the consultation and generally only present themselves at the advanced phase of their illnesses. Discharges against medical advice were mainly represented by desperate patients. This could be related to the fact that HIV-1 is the most widespread and responsible type of infection worldwide [21]. The CD4 count was very low in most of our patients; 59.68% had a CD4 count < 350/mm³. M.H. Ekat, *et al.* [16] in 2010 in Congo reported in their studies that 74.8% of patients had a CD4 count < 350 cells/mm³. M L Kaba, *et al.* [6] in 2016 in Guinea reported in their studies of 314 patients a CD4 count < 200/mm³ in 45% of cases. This result could be explained on the one hand by the delay in the diagnosis of HIV infection and the initiation of ARV treatment and on the other hand by the fact most of our patients consulted late, often at the advanced stage of their illnesses. Thirty-three of our patients, or 53.23%, were classified as stage III (WHO) of HIV infection. This result could also be justified by the delay in the diagnosis of HIV infection, the delay in starting ARV treatment and the late consultations of our patients, after having therefore allowed the disease to develop for a long time.

5. Conclusion

Kidney disease is very frequent and varied during HIV infection. While some are benign and reversible, others, on the contrary, are responsible for chronic kidney failure. The female sex was the most concerned with a predominance of young subjects. The most represented risk factors were increased exposure to nephrotoxic substances. The clinical manifestations of renal disease were mainly represented by glomerular nephropathy syndrome. Screening for kidney disease in the HIV population is therefore fundamental because its early diagnosis should allow the identification of patients at high risk of progression of kidney disease but also of hospitalization and mortality. Hence the importance of close collaboration between nephrologists and clinicians in charge of HIV infection.

Conflicts of Interest

All authors have read and approved the manuscript. They declare that there is no conflict of interest related to this work.

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