SciForschen
Open HUB for Scientific Research

International Journal of Nephrology and Kidney Failure

ISSN 2380-5498 | Open Access

RESEARCH ARTICLE

Volume 4 - Issue 2 | DOI: http://dx.doi.org/10.16966/2380-5498.158

Chronic Kidney Disease Related to Human Immunodeficiency Virus Infection and Acquired Immune Deficiency Syndrome: A Single Study an Madagascar

Ranivoharisoa EM[1*], Tongavelona J[2], Rabemiarason RN[1], Ramilitiana B[1], Randriamanantsoa LN[3], Randria MJD[2] and Randriamarotia WFH[1]

[1]Department of Nephrology and Hemodialysis Center, Befelatanana University Hospital, Antananarivo, Madagascar
[2]Department of Infectious Diseases, Befelatanana University Hospital, Antananarivo, Madagascar
[3]Department of Rea-Nephrology and Hemodialysis Center, Andranavolona University Hospital, Antananarivo, Madagascar

[*]**Corresponding author:** Ranivoharisoa EM, Department of Nephrology and Hemodialysis Center, Befelatanana University Hospital, Antananarivo, Madagascar, **E-mail:** remikmed@hotmail.fr

Received: 19 Feb, 2018 | **Accepted:** 30 Mar, 2018 | **Published:** 05 Apr, 2018

Citation: Ranivoharisoa EM, Tongavelona J, Rabemiarason RN, Ramilitiana B, Randriamanantsoa LN, et al. (2018) Chronic Kidney Disease Related to Human Immunodeficiency Virus Infection and Acquired Immune Deficiency Syndrome: A Single Study an Madagascar. Int J Nephrol Kidney Fail 4(2): dx.doi.org/10.16966/2380-5498.158

Abstract

Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) is a neglected cause of chronic kidney disease (CKD). The number of people infected by HIV/AIDS continues to rise in Africa. The goals of this study are to determine the prevalence of CKD related to HIV/AIDS in Madagascar and to determine the main risk factor. We conducted a retrospective and analytical study in single center analyzing HIV infected patients with CKD (Group 1) versus to control-group HIV infected patients without CKD (Group 2). The study was carried in the National Reference Center for the Diagnosis and Treatment of HIV/ AIDS Infection. All patients declared HIV-positive were included. Patients without the evaluation of the serum creatinine levels defining the state of the renal function were excluded.

At the end of the study, 115 patients were included with 36 patients in Group 1 and 79 patients in Group 2. The mean age in the cohort was 36.5 (± 9.8) years old with a sex-ratio 1.6. The time to appearing of symptoms and the positivity of HIV infection was on average 356 days. The major risk factors of HIV were the lack of using condom and the presence of multiple partners. The prevalence of CKD is 31.6% among HIV infected patients. In single variable logistic, analysis showed that HIV-related CKD was significantly related to age, a presence of an acute kidney injury with septic shock, and the CD4 serum levels. In multivariable logistic, it was significantly correlated with age over 50 years, blood pressure < 80 mmHg and body temperature > 38°2C and CD4 < 150 cells/µl. Older infected patients, severe immunodepression and presence of opportunistic infection and/or co-infection are risk factors of CKD leading to high morbidity and mortality. The management strategy should be primarily focused on information, education and behavior change to avoid this fatal infection.

Keywords: HIV; Tuberculosis; Chronic Kidney Disease -Madagascar

Introduction

Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) is a neglected cause of chronic kidney disease (CKD). In the United States, HIV Associated with Nephropathy (HIVAN) is the third cause of End-Stage of Renal Disease after diabetic and hypertensive nephropathy [1]. Despite it becomes a worldwide public health problem, there are few data available in some countries of Africa to highlight the particularities of CKD related to HIV/AIDS [2]. According to our knowledges, this is the first study conducted in Madagascar. There are several forms like HIV associated with nephropathy (HIVAN), Acute Kidney Injury (AKI) linked to antiretroviral (ARV) and CKD. The goals of this study are to determine the prevalence of CKD related to HIV and to determine the risk factors of HIV/AIDS, the main risk factors of CKD in order to improve the management of patients.

Patients and Methods

This is an observational, retrospective study in single center over a period of four-year between 01st of January 2011 and 31st of December 2015. We analyzed HIV infected patients

with CKD (Group 1) versus control-group HIV infected patients without CKD (Group 2). The study was carried out in the National Reference Center for Infection Diagnosis and Treatment of HIV/AIDS, in Madagascar.

As ethical considerations, the protocol of this study was submitted and accepted by the National Ethics Committees of the Ministry of Public Health. This Ethics Committees are the recipient of the final report of this study.

The collection of data was done with the agreement of the concerned patients and the Director of the Hospital.

We recruited all patients who accepted to do freely the HIV screening and who started treatment and have done medical followed-up in the same center. Malagasy patients declared HIV-positive were included. Patients without evaluation of renal function as creatinine serum level were excluded. Information consentment before HIV screening must be done and consisted to explain to each patient on the meaning and the objectives of the test. Each infected patient was asked if we could include his case in the study. There were a possibility that participant agree or disagree to be included. Patient's confidentiality and human rights were respected.

HIV screening was done systematically before: tuberculosis assessment, prenatal consultation, unexplained chronic fever, alteration of the general state but it may be also a volunteer screening.

All positive test must to be declared to patient.

We defined CKD if there was a gradual loss of kidney function and in biological test, there must be the presence of at least two plasma dosages of the serum creatinine spacing at least three months and confirming the irreversibility of kidney function.

The strip test Alere Determine HIV1/2 was used. It is a test that detects simultaneously HIV-1 and HIV-2 antibodies and free p24 antigens non-immunocomplexed HIV-1 (Ag). The test was "positive" when the strip is reactive with two appeared lines. All positive tests had to be confirmed by another UNI-GOLD test followed by dosing the CD4 serum level. Regarding the staging of HIV/AIDS and CKD, we have used the WHO (World Health Organization) classifications.

As parameters, we retained demographic characteristics mainly age and sex , personnel behaviors, clinical signs (risk factors for HIV, circumstances of infection discovery, co morbidities, hemodynamic parameters mainly blood pressure, temperature) and paraclinical signs (Hemoglobin, CRP, CD4 count, presence of opportunistic infections, co-infection, serum creatinine level), all medical treatment(using corticotherapy, tenofovir, HAART) and survival rate in 6-months after starting chimiotherapy.

Cohort was divided into two groups according to the presence or not of CKD. Group 1 collected all infected patients with CKD, group 2 all infected patients without CKD. Both two groups were treated and followed up in the same center. The National Protocol for HIV/AIDS treatment in Madagascar, Edition 2013 has been used.

Antiretroviral therapy has been initiated when the CD4 count is less than 500/mm3. Patients were classified as WHO Stage 3 and 4 in the presence of the following criteria whatever the level CD4 count: Hepatitis B and HIV co-infection, partner HIV/AIDS infected, a pregnancy or breastfeeding woman. The patients were followed-up during a period of 6 months.

At the first step of this study, we carried out a descriptive study. In a second step, we carried out an analytical study of all risk factors leading to the development of CKD.

As statistical test, the data was analyzed and processed by using the software Epi info version 7.1.3. The Odds Ratio (OR) was the measure to evaluate the relationship between independent and dependent variables. This OR was calculated with 95% confidence interval (CI). For the comparison of proportions, the Pearson Square Chi test was used, if the conditions of use were not fulfilled, the Fisher test was used. Result was statistically significant if p value ≤ 0.05.

Results

At the end of the study, 115 patients accepted to be included in this study with 36 patients in Group 1 and 79 patients in Group 2. The mean age in the cohort was 36.5 ± 9.8 years, with sex ratio 1.6.

In this study, the prevalence of CKD was 31.6% among HIV infected patients. General impairment and chronic fever and chronic cough were accounted respectively 43.5%, 34.8% and 7% of signs in hospital admission. Risk factors for HIV infection were mainly multiple partners (32%), lack of using condom (29%) and sexual transmitted infection (21%). The clinical, paraclinical, therapeutic and evolution characteristics of patients in both groups were summarized in Table 1.

Patients in group 1 were older compared to control group (p=0.0318). The CRP was similar between the two groups.

The delay on symptomatic signs and positivity of HIV test was on average 356 days in the cohort and longer in the control group (p=0.000000001). Several co-infections were found mainly syphilis (1.7%), hepatitis B (7%), hepatitis C (0.8%), and sexually transmitted infection (8%). Our study highlighted the prevalence of opportunist infection with 74% in cases of tuberculosis infection. Pulmonary form was encountered in 36.6% and extra pulmonary form was in 37.4%. Then, followed the cerebral toxoplasmosis (10.4%), oropharyngeal candidiasis (7.8%), pneumocystis carnii (6.6%) and cryptococcal meningitis (5.3%).

The presence of a septic shock was encountered in both group 1 and 2 respectively in 100% and 68.3%. According to the analytical statistic test, the level of CD4 in Group 1 was significantly lower than in the control group (168 cells/mm^3 *vs* 187 cells/mm^3). The viral charge was performed only in 4

Table 1: Patient characteristics (N = 115)

	Case-Group (1) N=36	Control-Group (2) N=79	$OR_{CI95\%}$	p-value
Genre Male Female	 31 (86.11%) 5 (11.63%)	 41 (51.9%) 38 (48.10%)	5.74 [2.02-16.30]	0.00016
Mean age (years) >50 <50	39.6 20 (55.5%) 16 (44.5%)	35.2 29 (36.7%) 50 (63.3%)	2.15 [1.06-4.80]	0.0318
Average duration between onset of symptoms and HIV discovery (days) <186 ≥ 186	142 21(58.3%) 15 (41.7 %)	432.4 0 (0%) 79 (100%)	NA	0.000000001
Average weight (Kg) <45 ≥ 45	45.4 17 (42.3%) 19 (52.7 %)	48.6 36 (45.5 %) 43 (54.5%)	1.06 [0.48-2.35]	0.435
Average size (mm) <158 ≥ 158	158 17 (42.3%) 19 (52.7 %)	159 39(43.8 %) 40(56.2%)	0.91 [0.41-2.02]	0.4174
Septic shock Presence Absence	 36 (100%) 0 (0%)	 54 (68.35%) 25 (31.65%)	NA	0.000000001
Average systolic blood pressure (mmHg) <80 ≥ 80	75 36 (100%) 0 (0%)	115 9 (11.39%) 70 (88.61%)	NA	0.000000001
Average heart rate (beats per minute) ≤ 80 >80	95 0 (0%) 36 (100%)	91 0 (0%) 79 (100%)	NA	0.07171
Average temperature (°C) <38°2 ≥ 38°2	38.2 1 (7.69%) 35 (92.31%)	37.6 27 (34.18%) 52 (65.82%)	23.11 [6.51-81;98]	0.00000003
Mean hemoglobin (g/dl) <13 ≥ 13	10.3 36 (100%) 0 (0%)	10.8 79 (100%) 0 (0%)	NA	0.017
Mean Creatininemia (µmol/L) <120 ≥ 120	231 0 (0%) 36 (100%)	73 79 (100%) 0 (0%)	NA	0.000000001
Average CRP (mg/l) ≤ 5 >5	60 0 (0%) 36 (100%)	65 0 (0%) 79 (100%)	NA	0.0171
CD4 means (cells/µl) <200 ≥ 200	168 36 (100%) 0 (0%)	187 49 (62%) 30 (38%)	NA	0.0171
Co-infections Presence Absence	 27 (75.00%) 9 (25.00%)	 26 (32.91%) 53 (67.09%)	6.11 [2.51-14.86]	0.00001
Opportunistic infections* Presence Absence	 22 (61.11%) 14 (38.89)	 10 (12.66%) 69 (87.34)	10.84 [4.22-27.83]	0.0000001
Corticosteroids Using Not using	 12 (33.33%) 24 (66.67%)	 27 (34.18%) 52 (65.82%)	0.96 [0.41-2.21]	0.468
HAART Using Not using	 21 (53.85%) 18 (46.15%)	 46 (53.23%) 33 (41.77%)	0.83 [0.38-1.81]	0.328
TENOFOVIR Using Not using	 21 (53.85%) 18 (46.15%)	 48 (60.76%) 31 (39.24%)	0.75 [0.34-1.63]	0.240
Survival rate Death Survival	 10 (25.64%) 26 (74.36%)	 17 (21.52%) 62 (78.48%)	1.25 [0.51-3.08]	0.309

NA : non applicable
OD : Odds Ration
CI : Confidence interval

patients with an average of 259336 copies/ml. The majority of patients (90.3%) were seen lately in advanced stages 3 and 4 of WHO Classification.

In mono variable logistic test, CKD was significantly related to the genre (man), the age, the presence of septic shock, and CD4 serum level. In multivariable test, it was significantly correlated with man, an age more than 50 years, a low blood pressure <80 mmHg and a high body temperature >38°2C and a low CD4 serum level <150 cells/mm^3.

In this study, we did not find a correlation between the occurrence of CKD and the use of nephrotoxic drugs including Tenofovir. Initiation treatment using antiretroviral therapy was encountered in 72.17% (n=83) of the cases. Among these, the HAART protocol was applied in 80.72% of the cases (n=67).

Concerning the main treatment of ESRD, two patients in group 1 were able to perform periodic dialysis. Unfortunately, they died after a septic shock. In 94.4%, the patients in ESRD were treating symptomatically. Evolution in 6-months follow-up was marked survival rate in 72.3% in group 1 compared to 78.5% in the control group.

Discussion

Our study represents the first study on the prevalence of CKD related to HIV/AIDS infection in Madagascar. But, it has some limitations including the absence of renal biopsy which can confirm and specify each nephropathy as HIVAN nephropathy, the retrospective character with few patients and the short follow-up time.

The prevalence of CKD related to HIV/AIDS infection differs from one country to another. According to CP Wen, et al. the prevalence of CKD in Taiwan represents 11.93% of the general population [3]. Min Han Hsieh, et al. [4] reported that among 1639 Taiwanese patients with CKD, only 36 had HIV-related infection which represents 7.03% of prevalence.

Compared to other African countries, CKD related to HIV/AIDS infection is a major cause of CKD in sub-Saharan Africa and accounts 27% of all causes [5]. One reported study in Abidjan analyzing 301 adults with CKD concluded that HIV-associated nephropathy accounted for 17% and takes the second cause of CKD after hypertensive nephropathy [6].

We can draw also from our results that CKD related to HIV/AIDS infection in Madagascar is not negligible. Chi Yuen Cheung, et al. [7] found that the predictive factors of an CKD in Chinese infected patients were older age, hypertension, diabetes, and a low CD4 count, Viral charge and use of Indinavir. Another study by Min-Han Hsieh, et al. [4] found that these factors are mainly advanced age, viral charge, high blood pressure, diabetes, exposure to antiretroviral and dyslipidemia. In our study, we found that CKD related to HIV/AIDS infection was significantly correlated with genre (man), age more than 50 years old, a high temperature more than 38°2C, an low blood pressure systolic less than 80 mmHg, and a low CD4 serum level less than 150/ml^3.

This may be related to the presence of a septic shock with an opportunist infection and co-infection due to late admission in hospital. In our study, any significant statistical correlation was found in using antiretroviral drugs as several studies have demonstrated [8,9]. This could be explained by our methodology which used the national protocol. In this protocol, all doses of the medicines were standardized and prescription of the dose of supposedly nephrotoxic drugs (Tenofovir) does not exceed 300 mg/d during each medication. The other drugs like Indinavir, dolutegravir were not yet included in this protocol. It is a low turnover drug because it is very expensive and its prescription is very rare in hospitalisation.

A particular point of our study was also the high prevalence of tuberculosis during CKD related to HIV/AIDS infection. Madagascar is a highly endemic area of tuberculosis. Tuberculosis has always been a high morbidity rate and its frequent association with HIV infection is known, or even worsened. According to an earlier study by Rakotoarivelo, et al. [10] among the 106 infected patients followed in the same center, 25 cases of tuberculosis were identified.

We also found a mortality rate of 27.7% during this study. High mortality could be related to an advanced stage of HIV/AIDS infection. The majority of patients were seen late in hospital (C3=90%) with complications of immunodepression as opportunistic infections which ultimate management is sometimes difficult [11]. In sub Saharan Africa, tuberculosis is responsible for a mortality rate of 21% in infected patients [12].

The specific part of the treatment known as HAART, combining three drugs (Tenofovir, lamivudine and Efavirenz) has completely changed the prognosis of HIV/AIDS patients. Several studies have demonstrated that the initiation of HAART significantly reduces the viral charge [13,14].

Other studies have reported that it can change the survival rate of patients [15,16]. In our cohort, we found that HAART prescription was found in 80.72% of cases. Unfortunately, our study could not demonstrate its efficacy on viral charge or patient survival. The duration of observation follow-up was short and the high cost of the laboratory analyzes carried out during the medical follow-up was in family charge and inaccessible to the majority of the patients.

In light of our study, CKD related to HIV/AIDS infection remains a major problem in Madagascar. Its association with tuberculosis is in aggravation. In order to avoid HIV/AIDS infection, we propose first of all an Information Education for the Change of Behaviors of Patients at high risk. Although medical treatment to HIV/AIDS and tuberculosis are free, the onset of advanced antiretroviral therapy does not seem to solve the problem. Individual awareness or mass awareness is needed to promote early screening. Follow-up by the State is essential to limit the complications of these co-infections. Systematic anti-tuberculosis prophylaxis could be discussed at some CD4 serum level.

Conclusion

CKD due to HIV/AIDS infection should not be a neglected cause of CKD in Madagascar. In this study, prevalence is high and represents 31.6%. Risk factors for HIV/AIDS were mainly the absence of condoms during sexual intercourse and the presence of multiple partners. The factors associated with the progression of CKD were man, advanced age, septic shock, and severe immunosuppression.

Tuberculosis, one of the most common opportunist infections, is responsible for high morbidity, including irreversible and speed decline of renal function with ESRD, sometimes compromising the patient's life prognosis.

The first step to avoid this fatal infection should focus on patient's education: abstinence, using condoms, and the treatment of sexually transmitted infections.

With the high endemicity of tuberculosis and HIV in Madagascar, we propose an earlier screening and systematic drug prophylaxis to limit severe complications. Our study represents a single study of CKD related to HIV/AIDS infection but it may represent national data awaiting further multiple centers and randomized studies.

References

1. Gupta SK, Eustace JA, Winston JA, Boydstun II, Ahuja TS, et al. (2005) Guidelines for the management of chronic kidney disease in HIV-infected patients: Recommandations of the HIV Medecine Association of the Infectious Disease Society of America. Clin Infect Dis 40:1559-1585.
2. Halle MP, Takongue C, Kengne AP, Kaze FF, Ngu KB (2015) Epidemiological profile of patients with end stage renal disease in a referral hospital in Cameroon. BMC Nephrol 16: 59.
3. Wen CP, Cheng TY, Tsai MK, Chang YC, Chan HT,et al. (2008) All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. Lancet 371: 2173-2182.
4. Hsieh MH, Lu PL, Kuo MC, Lin WR, Lin CY, et al. (2015) Prevalence of and associated factors with chronic kidney disease in human immunodeficiency virus-infected patients in Taiwan. J Microbiol Immunol Infect 48: 256-262.
5. Nestor-M P, Ernest-K S (2011) Anatomopathological features of renal disease in sub-Saharan Africa: a synthetic review of data from the Democratic Republic of the Congo "; Annales de Pathologie, Ann Pathol Artic under Press.
6. Bourhaima O, Ouffoue K, Hubert Y, Kouame K, Ezani Kodjo N (2011) Particularities of chronic renal disease in black adult patients hospitalized in the Department of Internal Medicine, Treichville University Hospital. Nephrol Ther.
7. Cheung CY, Wong KM, Lee MP, Liu YL, Kwok H, et al. (2007) Prevalence of chronic kidney disease in Chinese HIV-infected patients. Nephrol Dial Transplant 22: 3186-3190.
8. Jao J, Wyatt CM (2010) Antiretroviral Medications: Adverse Effects on the Kidney. Adv Chronic Kidney Dis 17: 72-82.
9. Valle R, Haragsim L (2006) Nephrotoxicity as a Complication of Antiretroviral Therapy. Adv Chronic Kidney Dis 13: 314-319.
10. Rakotoarivelo R, Tsifiregna R, Rberahona M, Randrianasolo R, Randria M (2012) Causes of death in HIV-infected patients in Madagascar. Rev Med Madag 2: 132-133.
11. Sansone GR, Frengley JD (2000) Impact of HAART on causes of death of persons with late-stage AIDS. J Urban Health 77: 166-175.
12. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R (2008) Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS 22: 1897-1908.
13. Moatti JP, Carrieri MP, Spire B, Gastaut JA, Cassuto JP, et al. (2000) Adherence to HAART in French HIV-infected injecting drug users: the contribution of buprenorphine drug maintenance treatment. The Manif 2000 study group. AIDS 14: 151-155.
14. Spire B, Duran S, Souville M, Leport C, Raffi F, et al. (2002) Adherence to highly active antiretroviral therapies (HAART) in HIV-infected patients: from a predictive to a dynamic approach. Soc Sci Med 54: 1481-1496.
15. Gabarre J, Philippe B (2003) HAART and modification of the epidemiology, treatment and prognosis of HIV-positif patients with Kaposi's disease and lymphoma. Bull Cancer 90: 419-25.
16. Milburn J, Jones R, Levy JB (2017) Renal effects of novel antiretroviral drugs. Nephron Dial Transplant 32: 434-439.