

Prevalence of Dilated Cardiomyopathy in HIV-Infected African Patients Not Receiving HAART: A Multicenter, Observational, Prospective, Cohort Study in Rwanda

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Abstract: *Introduction:* Several studies performed before the introduction of highly active antiretroviral therapy (HAART) have shown that HIV-1 infection is an important cause of dilated cardiomyopathy. However, factors associated with the development of HIV-associated cardiomyopathy in developing countries are still debated.

Objectives: To assess the prevalence of dilated cardiomyopathy, diagnosed by echocardiography, in HIV-infected Rwandese patients not receiving HAART and the risk factors associated with its development.

Methods: A sample of 416 HIV-infected african patients, without a previous definite history of cardiovascular disease, attending University hospitals in Rwanda, from January to December 2005, were included in a multicenter, observational, prospective, cohort study, with the collaboration of two European Clinical Centers (in France and in Italy). Clinical and laboratory tests along with echocardiographic examination were performed in all patients included in the study.

Results: Out of 416 patients included in the study, dilated cardiomyopathy was documented by echocardiography in 71 (17.7%). By both univariate and multivariate univariate analysis, low socio-economic status, estimated duration of HIV-1 infection, CD4 count, HIV-1 viral load, CDC stage B and C of HIV disease and low plasmatic level of selenium were factors significantly associated with the development of cardiomyopathy. Alcohol consumption and smoking were factors associated with the development of cardiomyopathy only by univariate analysis.

Conclusions: HIV-associated cardiomyopathy is a significant clinical problem in HIV-infected patients not receiving HAART in Rwanda. Early tracking of cardiomyopathy in african HIV-infected patients is therefore recommended. Before administering HAART, clinicians should be aware of a possible existing cardiomyopathy to ensure appropriate, comprehensive, and rational patient care.

Keywords: HIV-associated cardiomyopathy, HIV/AIDS, echocardiography, Africa, Rwanda.

INTRODUCTION

Cardiac manifestations in patients with Acquired Immunodeficiency Syndrome (AIDS) have been largely reported both in developed countries [6, 11, 12, 17], and in developing countries [8, 35, 41] before the introduction of highly active antiretroviral therapy (HAART). Various clinical manifestations have been described, including pericardial effusion, disturbances of the cardiac rhythm, malignant cardiac infiltration, marantic endocarditis, and cardiomyopathy [5, 46].

HIV-associated cardiomyopathy has a significant clinical importance in relation both to its prevalence and its impact on prognosis of AIDS patients [20, 23, 31]. Studies have shown that CD4 cell count alone cannot predict the survival rate in patients with AIDS; conditions such as dilated cardiomyopathy may become an important prognostic indicator, especially in developing countries, where the availability of HAART is scanty [6]. The importance of cardiac dysfunction is demonstrated by its effect on survival in AIDS. Median survival to AIDS-related death is 101 days in patients with left ventricular dysfunction and 472 days in patients with a normal heart by echocardiography at a similar infection stage [6].

Previous studies regarding dilated cardiomyopathy in patients with AIDS [1, 9, 11, 20, 37], as well as post-mortem

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series [16], have reported, both in adults and in children, a direct action on the myocardial muscle by HIV-1 itself or by opportunistic infectious agents or by malignancies (e.g. Kaposi's sarcoma, non-Hodgkin lymphoma). However, this does not fully explain why some patients have cardiac manifestations compared to others. Reports about the role of socio-economic status, nutritional status, CD4 count or HIV-1 viral load still remain limited. Especially in developing countries, where diagnostic tools are scanty, HIV-infected patients have not an easy access to an accurate clinical and laboratory evaluation [42]. In these conditions, it is important to assess the prevalence of HIV-associated cardiomyopathy and the possible risk factors which may be predictor of its development [42]. This should help to set up recommendations and clinical guidelines for a better management of HIV/AIDS patients.

Up to now, no study on the prevalence of HIV-associated cardiomyopathy has been performed in Rwanda. Aim of this study has been to assess the prevalence of HIV-associated cardiomyopathy and the clinical and laboratory parameters possibly implicated in its development in Rwandan HIV/AIDS patients not receiving HAART.

PATIENTS AND METHODS

Study Population

We report the preliminary results of a multicenter, observational, prospective cohort study, performed in Rwanda, from January to December 2005, with the collaboration of two European Clinical Centers (in France and in Italy). The study sampled HIV-infected African black patients attending two University hospitals in Rwanda (University Teaching Hospital of Butare, and University Teaching Hospital of Kigali). The study includes 416 consecutive HIV-infected patients consulting internal medicine departments for clinical assessment before starting HAART. The inclusion criteria were: positive serology for HIV-1, and the absence of a previous definite (non-HIV-associated) cardiovascular disease according to the documented clinical records. The study was approved by hospitals' Institutional Review Board and all patients included in the study provided informed consent.

Study Procedures

For each patient clinical examination and biochemical investigations (including CD4 count, HIV-1 viral load, plasma selenium level) were performed. Lymphocyte typing was obtained automatically using a flow cytometer (Facscount Becton Dickinson, Franklin Lake, NJ). HIV-1 RNA in plasma was measured by the Amplicor HIV-1 Monitor test with Ultra sensitive Specimen Preparation (Roche Molecular Systems, Pleasanton, CA). Plasma samples with undetectable HIV-1 RNA were assigned the detection limit of 50 copies/mL. All laboratory investigations were gathered in the same place, and analysis were carried out by local trained team, but for HIV-1 viral load and for plasma selenium level the samples were sent abroad. Every patient underwent M-B-mode echocardiography (Hewlett-Packard, Palo Alto, CA). Echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography [45]. Echocardiographic

images, stored in videotapes, were read by two echocardiographic readers who were blinded to patients' clinical status. The coefficient of variation between the two different echocardiographic readers was 1.8%, indicating good reproducibility of the echocardiographic measurements. Echocardiographic diagnosis of dilated cardiomyopathy was based on the presence of diffuse left ventricular hypokinesia (ejection fraction < 45%) and left ventricular dilatation (left ventricular end-diastolic volume index > 80 ml/m²) [18, 28, 29, 38].

Statistical Analysis

Continuous data, which were expressed as means \pm standard deviation, were analysed by Student's t test. The chi-square test with Yates' correction and Fisher's exact test were used for analysis of categorical data. The associations between continuous variables were assessed either by Spearman rank test or by Pearson correlation test. Univariate and multivariate analysis were performed to examine the association between clinical and laboratory variables and the development of HIV-associated cardiomyopathy. Only variables that were significant at an alpha level of 0.05 in the univariate analyses were included in the multivariable analysis. The odd ratio, with related 95% confidence intervals (95% CI) was calculated for each variable in the final model. All data transformations and analysis were two-tailed and were performed with Epi-Info software (version 6, CDC, Atlanta, GO), and SPSS for Windows software (SPSS 12.0 Inc., Chicago, IL).

RESULTS

Baseline Patient Characteristics and Prevalence of Cardiomyopathy

Out of 416 HIV-infected patients included in the study, echocardiographic diagnosis of dilated cardiomyopathy was made in 71 (17.7%; 95% CI: 13.6% to 21.1%). The baseline characteristics of the patients included in the study are reported in Tables 1 and 2.

The age of the patients included in the study ranged between 19 years and 61 years with a mean of 34.60 years \pm 6.96. 47.8% of HIV-infected patients were aged between 36 and 45 years, and 38.7% were aged between 46 and 55 years. Of 71 patients with echocardiographic diagnosis of cardiomyopathy, 31 (43.7%) were aged between 26 and 35 years, and 25 (35.2%) were aged between 36 and 45 years. Blood lymphocyte counts and HIV-1 viral load of the patients included in the study, with or without cardiomyopathy, are reported in Table 3.

Blood Lymphocyte Counts, HIV-1 Viral Load and Cardiomyopathy

In the group of HIV-infected patients with cardiomyopathy, the mean CD4 count was 145/mm³ compared to 210/mm³ in patients without cardiomyopathy ($p < 0.001$); the mean total lymphocyte count was 1317/mm³ versus 1784/mm³ ($p < 0.001$); the mean CD8 count was 854/mm³ versus 864/mm³ ($p = 0.555$). HIV-1 plasma viral load was higher in patients with cardiomyopathy compared to those without cardiomyopathy: 5.59 ± 0.47 and 4.69 ± 0.35 log₁₀ copies/ml, respectively ($P < 0.001$). HIV-1

Table 1. Baseline Characteristics (Quantitative Variables) of the 416 Patients Included in the Study

Parameters	Mean	Std. Deviation	Minimum	Maximum
Age (Years)	34.6	7.0	19	61
Weight (Kilograms)	59.0	8.9	45.0	81.0
Height (Centimeters)	165.9	3.7	157.6	176.0
Body mass index (Kg/m ²)	21.4	3.0	15.4	28.0
Body surface (m ²)	1.6	0.1	1.420	1.966
Duration of known positive HIV serology (days)	164.4	116.6	30	1.460
Estimated duration of illness since contamination (Days)	712.0	679.1	150	3.650
Heart rate (beats/min)	89.4	16.4	40	144
Systolic Blood Pressure (mmHg)	122.8	8.1	95	139
Diastolic Blood Pressure (mmHg)	65.9	8.6	49	87
White blood cells (Cells/mm ³)	3976.1	1361.0	950	5600
Total lymphocytes (Cells/mm ³)	1.705.1	771.7	148	3841
CD4 (Cells/mm ³)	199.5	92.6	2	400
CD8 (Cells/mm ³)	863.0	131.6	190	1.018
CD4/CD8	0.241	0.121	0.002	0.966
Log ₁₀ of Viral load	4.984	0.573	3.672	6.464
Blood Glucose (mg/dl)	87.9	14.2	55.0	117.0
Plasmatic Lactate Deshydrogenase Enzyme (mg/dl)	210.4	71.8	79.0	456.0
Plasmatic creatinin level (mg/dl)	0.5	0.4	0.0	1.5
Plasmatic natriuretic level (mmol/dl)	131.5	3.5	125.0	136.0
Plasmatic Potassium level (mmol/dl)	5.3	0.6	4.0	6.4
Plasmatic Selenium (micro-mol/L)	0.891	0.327	0.205	1.608
Hemoglobin concentration (g/dl)	8.6	2.6	3.3	12.6
Plasmatic Creatin Phospokinase Myocardial (UI/L)	4.5	3.1	0.3	16.8
Total plasmatic cholesterol (mg/dl)	226.3	69.5	90.0	407.0
Low density lipoprotein cholesterol in blood (mg/L)	39.5	28.6	3.9	224.3
Tryglyceridemia (mg/dl)	176.7	60.6	47.0	327.0
Left Ventricular Mass index (g/m ²)	120.0	38.5	46.9	321.3

plasma viral load was inversely correlated to CD4 cell count ($r = 0.188$; $P=0.005$), to total white blood cell count ($r=0.187$; $P=0.005$), but not to total lymphocyte count ($r = 0.126$; $P=0.060$). There was a significant correlation between total lymphocyte count and CD4 count ($r = 0.286$; $P<0.001$).

Estimated Duration of HIV Infection and Cardiomyopathy

There was a significant relationship between the estimated duration of HIV infection and cardiomyopathy. In the group of patients with cardiomyopathy the mean estimated duration of HIV infection was 1356 days compared to 579 days in patients without cardiomyopathy ($p<0.001$). The estimated duration of HIV infection was inversely correlated to CD4 count ($r = 0.203$; $P< 0.001$), to total white blood cell count ($r = 0.374$; $P<0.001$) and to total lymphocyte count ($r = 0.335$; $P<0.001$).

Risk factors associated with development of HIV-associated cardiomyopathy

Univariate Analysis

With univariate analysis, the following factors were associated with development of HIV-associated cardiomyopathy: low socio-economic status, estimated duration of HIV infection, Center for Disease Control and Prevention (CDC) stage B and C of HIV disease, low plasmatic level of selenium, HIV-1 viral load, CD4 count, alcohol consumption, smoking and wasting syndrome and some opportunistic infections, such as "more than two opportunistic, tuberculosis (TB) not included", candidiasis and pericarditis (Tables 4a, b).

Multivariate Analysis

With multivariate analysis, only seven parameters were associated with cardiomyopathy: socio-economic status,

Table 2. Baseline Characteristics (Qualitative Variables) of the Patients Included in the Study with or Without Echocardiographic Diagnosis of Cardiomyopathy

Parameters		Cardiomyopathy (n=71)		No cardiomyopathy (n=345)		Total	
		Freq.	% in this group	Freq.	% in this group	Freq.	% in 416 subjects
Sex	Female	21	29.6	137	39.7	158	38.0
	Male	50	70.4	208	60.3	258	62.0
Age group in years	16 to 25 years	9	12.7	29	8.4	38	9.1
	26 to 35 years	31	43.7	168	48.7	199	47.8
	36 to 45 years	25	35.2	136	39.4	161	38.7
	46 to 55 years	3	4.2	8	2.3	11	2.6
	56 to 65 years	3	0.0	4	2.3	7	1.7
Economic status (Based on Income, profession and family size)	High	9	12.7	45	13.0	54	13.0
	Medium	11	15.5	99	28.7	110	26.4
	Low	51	71.8	201	58.3	252	60.6
Smoking	Yes	50	70.4	103	29.9	153	36.8
Alcohol use	Yes	57	80.3	187	54.2	244	58.7
Lack of physical activity	Yes	39	54.9	127	36.8	166	39.9
Thoracic pain	Yes	30	42.3	100	29.0	130	31.3
Cardiac palpitations	Yes	14	19.7	72	20.9	86	20.7
Headache	Yes	42	59.2	300	87.0	342	82.2
Cough	Yes	50	70.4	48	13.9	98	23.6
Dyspnea	Yes	35	49.3	58	16.8	93	22.4
NYHA* Classification	NYHA Stage I	19	26.8	48	13.9	67	16.1
	NYHA Stage II	11	15.5	6	1.7	17	4.1
	NYHA Stage III	3	4.2	4	1.2	7	1.7
	NYHA Stage IV	2	2.8	0	0.0	2	0.5
Hemoptysis	Yes	38	53.5	23	6.7	61	14.7
Lower limb oedema	Yes	8	11.3	10	2.9	18	4.3
Systolic cardiac murmur	Yes	6	8.5	9	2.6	15	3.6
Diastolic cardiac murmur	Yes	6	8.5	9	2.6	15	3.6
Systo-diastolic cardiac murmur	Yes	6	8.5	10	2.9	16	3.8
Pulmonary crepitation	Yes	25	35.2	45	13.0	70	16.8
Opportunistic infections	None	41	57.7	251	72.8	292	70.2
	Candidiasis	0	0.0	26	7.5	26	6.3
	PCP	1	1.4	5	1.4	6	1.4
	Tuberculosis	0	0.0	1	0.3	1	0.2
	Wasting	4	5.6	3	0.9	7	1.7
	More than two opportunistics, TB not included	19	26.8	30	8.7	49	11.8
	More than two opportunistics, TB included	4	5.6	7	2.0	11	2.6
	Others	3	4.2	22	6.4	25	6.0
CDC stage of HIV disease (CDC 1993)[10]	Stage A	6	8.5	106	30.7	112	26.9
	Stage B	45	63.4	191	55.4	236	56.7
	Stage C	20	28.2	48	13.9	68	16.3

*NYHA = New York Heart Association.

Table 3. Blood Lymphocyte Counts and HIV-1 Viral Load in HIV Infected Patients With and Without Echocardiographic Diagnosis of Dilated Cardiomyopathy

	Cardiomyopathy	Mean	Std. Deviation	P-value
White blood cells (Cells/mm ³)	Yes	3396, 20	1340, 77	<0.001*
	No	4095, 42	1336, 14	
Total lymphocytes (Cells/mm ³)	Yes	1317, 60	655, 92	<0.001
	No	1784, 90	770, 39	
CD4 (Cells/mm ³)	Yes	145, 25	75, 44	<0.001
	No	210, 63	92, 01	
CD8 (Cells/mm ³)	Yes	854, 11	155, 97	N.S.
	No	864, 88	126, 18	
CD4/CD8	Yes	0, 19	0, 11	<0.001
	No	0, 25	0, 12	
HIV-1 Log ₁₀ of Viral load	Yes	5, 59	0, 47	<0.001
	No	4, 70	0, 35	

*Mann – Whitney U test.

N.S.: Not statistically significant.

Table 4a. Univariate Analysis for Qualitative Variables

		Cardiomyopathy (n=71)		No cardiomyopathy (n=345)		Statistics	
		Frequencies		Frequencies		OR (95% CI) P-Value	
Risk factors and predictors							
Gender	Female	21	137	0.64 (0.35-1.15) N.S.			
	Male	50	208	1.57 (0.87 – 2.83) N.S.			
Age group in years	16 to 25 years	9	29	1.58 (0.66 – 3.70) N.S.			
	26 to 35 years	31	168	0.85 (0.49 – 1.46) N.S.			
	36 to 45 years	25	136	0.84 (0.47 – 1.47) N.S.			
	46 to 55 years	3	8	1.86 (0.38 – 7.96) N.S.			
	56 to 65 years	3	4	0.38 (0.06 – 2.14) N.S.			
Economic status (Based on Income, profession and family size)	High	9	45	0.97 (0.42 – 2.19) N.S.			
	Medium	11	99	0.46 (0.22 – 1.09) N.S.			
	Low	51	201	1.83 (1.01 – 3.32) 0.033			
Smoking	Yes	50	103	5.59 (3.09 – 10.18) <0.001			
Alcohol use	Yes	57	187	3.44 (1.78 – 6.73) <0.001			
Lack of physical activity	Yes	39	127	2.09 (1.21 – 3.63) 0.005			
Other opportunistic infections							
Pericarditis	Yes	18	52	1.91 (1.00 – 3.67) 0.035			
Other Opportunistic infections	None	41	251	0.51 (0.29-0.90) 0.011			
	Candidiasis	0	26	* 0.013			
	PCP	1	5	* N.S.			
	Tuberculosis (TB)	0	1	* N.S.			
	Wasting	4	3	10.55 (2.27 – 54.81) <0.001			
	More than two opportunistics, TB not included	19	30	3.84 (1.92 – 7.66) <0.001			
	More than two opportunistics, TB included	4	7	2.88 (0.69-11.3) N.S.			
CDC stage of HIV disease	Others	3	22	0.65 (0.15 – 2.37) N.S.			
	Stage A	6	106	0.21 (0.08-0.52) N.S.			
	Stage B	45	191	7.36 (2.58 – 22.03) <0.001			
	Stage C	20	48	4.16 (1.63 – 11.24) 0.001			

*No calculations possible.

N.S. Not statistically significant.

Table 4b. Univariate Analysis for Quantitative Variables

Parameters	Cardiomyopathy	Mean	Std. Dev.	p-value
Age (years)**	Yes	35.28	8.19	N.S.
	No	34.46	6.69	
Estimated duration of illness since contamination (days)**	Yes	1.356.34	873.85	<0.001
	No	579.42	545.52	
Body mass index (Kg/m ²)	Yes	22.11	2.90	0.036
	No	21.29	3.00	
Body surface (m ²)	Yes	1.67	0.11	N.S.
	No	1.65	0.12	
Systolic Blood Pressure (mmHg)*	Yes	121.76	10.35	N.S.
	No	122.98	7.58	
Diastolic Blood Pressure (mmHg)	Yes	67.58	9.30	N.S.
	No	65.50	8.39	
White blood cells (Cells/mm ³)**	Yes	3396.20	1340.77	<0.001
	No	4095.42	1336.14	
Total lymphocytes (Cells/mm ³)*	Yes	1317.60	655.93	<0.001
	No	1784.90	770.39	
CD4 (Cells/mm ³)*	Yes	145.25	75.44	<0.001
	No	210.63	92.01	
CD8(Cells/mm ³)	Yes	854.11	155.98	N.S.
	No	864.88	126.18	
Log ₁₀ of Viral load*	Yes	5.59	0.47	<0.001
	No	4.70	0.35	
Plasmatic creatinin level (mg/dl)**	Yes	0.53	0.40	N.S.
	No	0.530	0.39	
Plasmatic natriuretic level (mmol/dl)	Yes	131.51	3.61	N.S.
	No	131.48	3.53	
Blood Glucose (mg/dl)	Yes	84.56	13.712	0.030
	No	88.57	14.213	
Plasmatic Lactate Deshydrogenase Enzyme (mg/dl)	Yes	187.58	66.577	0.003
	No	215.12	71.98	
Plasmatic Potassium level (mmol/dl)	Yes	5.23	0.62	N.S.
	No	5.27	0.55	
Plasmatic Selenium (micro-mol/L)*	Yes	0.55	0.34	<0.001
	No	1.02	0.20	
Hemoglobin concentration (g/dl)	Yes	5.15	1.83	<0.001
	No	9.32	2.10	
Plasmatic Creatin Phospokinase Myocardial (UI/L)	Yes	5.78	3.12	<0.001
	No	4.20	2.98	
Total plasmatic cholesterol (mg/dl)	Yes	231.32	69.05	N.S.
	No	225.24	69.61	
Low density lipoprotein cholesterol in blood (mmol/L)*	Yes	1.3744	0.34	<0.001
	No	0.9474	0.78	
Tryglyceridemia (mg/dl)*	Yes	163.50	66.14	N.S.
	No	179.37	59.09	

*Equal variances not assumed (Levene's Test for Equality of Variances, p<0.05).

** Mann – Whitney U test.

N.S. : Not statistically significant.

estimated duration of HIV infection, CDC stage B and C of HIV disease, total lymphocyte count, CD4 count, HIV-1 viral load and low plasmatic level of selenium (Table 5).

DISCUSSION

HIV-associated cardiomyopathy have not attracted much attention in the African clinical settings. This may be partly justified by the fact that the clinical picture of HIV disease is dominated by opportunistic infections and malignancies focusing on them the interest by african health care providers [43]. Moreover, the diagnostic tools in these clinical settings are scanty and this may have underestimated the real prevalence of HIV-associated cardiomyopathy over time. According both to the literature review by Magula *et al.* [36] and to cross-sectional and retrospective studies [21, 33] HIV-associated cardiomyopathy is the leading cause of heart disease and death for congestive heart failure in Africa.

HIV-associated cardiomyopathy is characterized by global systolic functional impairment with or without left ventricular dilatation [36]. According to one retrospective study, the overall hospital mortality rate of HIV-infected patients with cardiomyopathy in Africa has been estimated to be about 5%[41]. Magula *et al.* report a 28% prevalence of cardiomyopathy in HIV-infected african outpatients [36]; this prevalence is higher than that reported in our study (17.7%). However, the prevalence reported by us is within the range reported by previous studies [25, 36, 42, 43].

Studies that examined the cause of cardiomyopathy in HIV-infected people living in Africa are limited. Magula *et al.* [36] report the histopathological findings of 16 HIV-infected patients with cardiomyopathy in a cohort of 157 patients [33]. In this report, all 16 patients with cardiomyopathy had histopathological findings of acute myocarditis. Myocarditis was attributed to *Toxoplasma gondii* infection in 3 cases (18.75%), to *Cryptococcus neoformans* infection in 3 cases(18.75%), to *Mycobacterium avium intracellulare* infection in 2 cases (12.5%), and to a direct HIV-1 infection in 8 cases (50%). These results suggest that HIV-associated cardiomyopathy may be caused by potentially treatable opportunistic infections in up to 50% of patients living in the sub-Saharan region [36]. By contrast, in Western series, opportunistic cardiotropic viral infections have

been implicated in a significant proportion of cases [4, 19, 22, 24, 26, 27, 39, 47].

Most of the patients in our study were free of specific cardiovascular signs and symptoms. This finding, which is in agreement with that reported by Nzuobontane *et al.* in Cameroon [43] and by Longo-Mbenza in Kinshasa [33], indicates that cardiac abnormalities in HIV-infected african patients are clinically discrete. The significant association of cardiomyopathy with a low CD4 count and an high HIV-1 viral load as documented in our study, by both univariate and multivariate analysis, suggests that the development of cardiomyopathy is correlated to the state of immunodepression of the patients. This finding, which is significantly correlated to the socio-economic status of the patients, is in agreement with that reported both in african and in non-african series [3, 34, 43].

The HIV/AIDS pandemic in Rwanda emerged in a special context of poverty where about 60% of Rwandese population live under the poverty line [4, 14]. The link between poverty and HIV/AIDS in Africa is well known. The socio-economic status and the nutritional status (especially selenium deficiency) may play a significant role in the development of HIV-associated cardiomyopathy in Rwanda.

In our study population selenium deficiency, correlated to a low socio-economic status of the patients, was significantly associated with the development of cardiomyopathy, both in univariate and in multivariate analysis. Selenium deficiency is believed to be the cause of Keshan’s disease, a form of dilated cardiomyopathy described in China [40, 48], but only rarely reported in the United States [15]. The role of selenium deficiency in the development of HIV-associated cardiomyopathy and the mechanism by which selenium protects the heart muscle from viral damage is still controversial. Kaul *et al.* [7, 32], Beck *et al.* [7], and Chariot *et al.* [11] suggest that it may be related to the antioxidant properties of selenium. Virus attacks (eg, by coxsackievirus B3 or HIV-1 itself) can cause the release of free radicals. Selenium may neutralize the effect of free radicals, preventing cardiac damage. Studies comparing populations in parts of the world other than China have not supported a link between selenium deficiency and dilated cardiomyopathy [30, 44], except in Taiwan [13]. Moreover, no

Table 5. Multivariate Analysis

Risk factors associated with Cardiomyopathy	B	S.E.	Wald	p-Value	Exp (B)	95, 0% C.I.for EXP (B)	
						Lower	Upper
Low Socioeconomic status (Based on Income, profession and family size)	1.24	0.36	11.97	0.001	3.47	1.71	7.01
Estimated duration of HIV infection in days	0.59	0.05	138.63	<0.001	1.81	1.64	2.00
Total lymphocytes counts (Cells/mm ³)	1.49	0.38	15.18	<0.001	4.44	2.10	9.39
CD4 (Cells/mm ³)	0.63	0.05	135.51	<0.001	1.88	1.69	2.09
Log ₁₀ Viral Load (RNA-Copies/mm ³)	0.96	0.34	8.06	0.005	2.61	1.35	5.07
Plasmatic level of selenium (micro-mol/L)	0.65	0.05	142.74	<0.003	1.92	1.73	2.14
CDC stage B of HIV disease	1.21	0.35	13.44	<0.001	3.34	1.50	8.12
CDC stage C of HIV disease	1.19	0.35	10.01	<0.001	2.89	1.47	6.77

clinical trials outside of China have explored the effects of selenium supplementation in patients with dilated cardiomyopathy. However, HIV-associated cardiomyopathy is not Keshan disease [2]. Because of its multifactorial etiology, it is clear that selenium deficiency alone would not explain the development of cardiomyopathy, since it may contribute to the development of cardiomyopathy in association with other factors correlated with the socio-economic status of the patients, such as duration of HIV infection, CD4 count and HIV-1 viral load. Anyway, selenium deficiency should be carefully checked in african HIV-infected patients with dilated cardiomyopathy, especially in those with a low socio-economic status, since supplementation may have a possible therapeutic role in improving the cardiac morpho-functional parameters. Controlled clinical studies on this topic are needed.

CONCLUSIONS

HIV-associated cardiomyopathy is a significant clinical problem in HIV-infected patients not receiving HAART in Rwanda. According to our study, HIV-associated cardiomyopathy is significantly associated with a low socio-economic status, with a longer duration of HIV infection, with a low total lymphocyte count, with a low CD4 count, with an high HIV-1 viral load and with low plasmatic levels of selenium. A careful echocardiographic screening is needed in patients with documented long duration of HIV infection and low socio-economic status, even with absent or mild signs and symptoms of cardiac disease. Early detection of cardiomyopathy in patients with HIV is therefore highly recommended. Before introducing HAART, clinicians should be aware of a possible existing cardiomyopathy to ensure appropriate, comprehensive, and rational patient care.

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