

Cardiovascular Diseases in HIV-Infected Patients at Kamenge Teaching Hospital in **Burundi**

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Abstract

Introduction: HIV-positive individuals are more prone to developing cardiovascular disease because of HIV-specific and non-traditional risk factors. This study aimed to describe cardiovascular diseases associated with HIV/AIDS in low-income settings. Materials and methods: The study conducted at Kamenge Teaching Hospital in Burundi, from January 2022 to December 2023 was a prospective, observational study aimed at providing clinical and descriptive insights into HIV-infected patients receiving ARV medication, focusing on cardiovascular disease, positive HIV serology, and no prior cardiovascular disease. Results: This study included 38 participants with cardiovascular disease from 115 HIVinfected patients (33.04 %). Our study included 26 (68.42%) women and 12 (31.58%) men. Their mean age was 48.60 ± 11.58 years. Widowhood was associated with cardiovascular disease in HIV-infected patients in our study, as indicated by the statistical analysis (p = $0.0171, \chi 2 = 9.6611$ for CI = 95%). In our comprehensive study of cardiovascular diseases, deep vein thrombosis (DVT) emerged as the predominant condition, accounting for 34.21% of cases, followed by dilated cardiomyopathy at 28.95%. Valvular heart disease (21.05%), ischemic heart disease (18.42%), hypertension (15.79%), pericarditis (13.16%), and stroke and pulmonary arterial hypertension (7.89%) were also observed. Furthermore, pulmonary embolism and arrhythmia-induced cardiomyopathy were present in 2.63% of the study participants. Conclusion: Cardiovascular diseases are diverse among patients with HIV infection. The most prevalent complications were deep vein thrombosis of the lower limbs, followed by dilated cardiomyopathy, valvular cardiomyopathy, ischemic cardiomyopathy, and hypertension, which caused heart failure in young people with severe immunosuppression.

Keywords: Novel drug delivery system, Therapeutic dose, Pharmacokinetic, pharmacodynamic

1. Introduction

The majority of data on HIV and clinical cardiovascular disease are from developed countries, especially Europe and North America, with an estimation of 37.9 million people living with HIV in total, of them 25.6 million are living in Sub-Saharan Africa ^[1, 2]. HIV-infected patients who receive life-saving combination antiretroviral therapy (ART) may have a higher risk of age-related illnesses, including cardiovascular diseases. The average age of HIV patients receiving ART is increasing and will rise from 43.9 years in 2010 to 56.5 years in 2030, with 78% of HIV patients having cardiovascular disease ^[3]. Currently, most countries in sub-Saharan Africa have implemented a policy of treating all HIV-positive people to ensure timely antiretroviral therapy ^[4].

Due to the availability of antiretroviral treatment, people living with HIV (PLHIV) will live longer than before, and their number is expected to triple by 2040 for those aged 50 years or older in Sub-Saharan Africa ^[5].

HIV-positive individuals are more likely to develop cardiovascular disease than those without HIV, driven by age; increased survival; and traditional, non-traditional, HIVspecific, and antiretroviral therapy risk factors ^[6]. Traditional risk factors include hypertension, diabetes, smoking, biological sex and dyslipidemia ^[7]. Exposure to these risk factors significantly increases the risk of cardiovascular disease independent of HIV status [8]. HIV-related processes that contribute to cardiovascular disease include inflammatory effects from HIV proteins, depletion of CD4+ T cells, increased intestinal permeability, microbial translocation, and altered lipid metabolism. HIV-infected patients have higher levels of biomarkers of monocyte activation, chronic inflammatory processes, and coagulation disorders than those without HIV ^[9]. A disordered coagulation system may accompany these inflammatory alterations and lead to venous thromboembolism such as deep vein thrombosis (DVT) ^[10]. Weakened adaptive immunity can lead to opportunistic infections, causing a chronic inflammatory response, potentially leading to cardiovascular diseases ^[11]. Cardiac disorders caused by HIV infection are common and can cause structural and functional damage through complicated pathways, such as direct infection of heart tissue. The severity of immunodeficiency and opportunistic infections play a key role ^[12]. HIV attacks the entire human body and cardiovascular system, including other vital organs of the body, such as the kidneys. The prevalence of HIV-associated nephropathy varies worldwide. with the highest rates occurring in sub-Saharan Africa^[13].

As the survival of people with HIV increases, their comorbidities become increasingly difficult for healthcare systems in low-income countries to handle efficiently ^[14]. Over the last few years, there has been a shift in focus from communicable to non-communicable disease management for people living with HIV ^[15]. The increase in the life expectancy of HIV-infected people in developed countries raises concerns that in the coming years, it will increase the incidence of cardiovascular events such as coronary events in aging HIV-infected patients ^[16].

The problem that led us to conduct our research is that HIV/AIDS is one of the most frequent diseases in patients hospitalized in Burundi's hospitals. In addition, cardiovascular diseases (CVD) are the leading cause of death worldwide and the situation is worsening in HIV+ patients due to the multiplicity of risk factors. The objective of our study was to describe cardiovascular diseases during HIV/AIDS infections. In Burundi, no such study has been conducted to evaluate or describe cardiovascular diseases in HIV-infected patients. Knowledge of cardiovascular complications in HIV-positive patients will allow healthcare providers to screen for their occurrence and apply preventive or therapeutic measures to reduce morbidity and mortality.

2. Materials and methods

2.1. Study population and data collection

The study conducted at Kamenge Teaching Hospital in Bujumbura, Burundi, from January 2022 to December 2023 was a prospective, observational study aimed at providing clinical and descriptive insights into HIV-infected patients receiving antiretroviral medication. The patients were

monitored in the Internal Medicine department. Data collection involved hospitalized individuals meeting specific inclusion criteria, which included progressive cardiovascular disease, positive HIV serology, no known history of cardiovascular diseases before HIV infection, and current course of ARV treatment. A definitive diagnosis of cardiovascular pathology was established by meticulous review of various sources of information. Medical history was examined to understand the evolution of HIV infection, associated conditions, cardiovascular risk elements, and ongoing therapeutic regimens. Physical examination was crucial to identify observable signs indicative of cardiovascular implications. Imaging and laboratory analyses were performed to detect possible abnormalities in the cardiovascular system. All these measures were essential in painting a comprehensive picture of the cardiovascular health status of HIV-infected individuals undergoing antiretroviral therapy at the hospital. In this study, a comprehensive analysis was conducted on a range of variables, including assessing factors such as age, sex, occupation, and origin, as well as examining various clinical and paraclinical data. These data encompassed the results of standard chest X-ray imaging, electrocardiography readings, echocardiography images, Doppler ultrasound scans of the lower limbs, brain computed tomography findings, and measurements of certain biological elements. Transthoracic echocardiography, a noninvasive imaging technique, was conducted in twodimensional mode using the TM-mode accompanied by color Doppler imaging. This comprehensive assessment method enables the evaluation of various crucial aspects of the cardiovascular system, including the examination of parietal and segmental kinetics, assessment of the pericardium, detailed inspection of valve structures, and precise measurement of the dimensions of key cardiac chambers, such as the left atrium, left and right ventricles, and the pulmonary artery. Additionally, vital cardiac functional parameters, such as left ventricular shortening and ejection fraction, were meticulously calculated and analyzed during echocardiographic assessment. In addition to cardiac evaluation, Doppler ultrasound has been used to screen for deep vein thrombosis (DVT) in the lower limbs by proficient healthcare professionals, such as emergency medicine physicians, cardiologists, radiologists, or other skilled clinicians with expertise in ultrasound imaging. Moreover, in cases exhibiting clinical manifestations suggestive of stroke, a brain CT scan was promptly performed to identify any intracranial hemorrhage or cerebral tissue damage resulting from stroke. Diagnostic investigations further encompassed an array of laboratory parameters essential for comprehensive patient evaluation, including tests for complete blood count (CBC), CD4 count, viral load, serum creatinine, blood urea levels, blood glucose, lipid profile, D-dimer, and electrolyte balance.

2.2. Data analysis

In the subsequent analytical phase, the collected data were meticulously processed using IBM SPSS 25 software, utilizing statistical tools such as chi-square and independence tests to determine the interrelationship between key variables. The significance level for establishing statistical relevance was set at a p-value < 0.05, indicating rejection of the null hypothesis (H0) in support of the alternative hypothesis (H1), which signifies a nonuniform distribution of traits across the population under study. To preserve the null hypothesis (H0), a p-value exceeding 0.05 was considered.

3. Results

3.1. Sociodemographic characteristics

During the study period, 115 patients were living with HIV infection. Among the PLHIV, we recorded 38 patients who met the inclusion criteria (33.04%). The study sample comprised 38 patients, with 26 females (68.42%) and 12 males (31.58%), resulting in a sex ratio (women/men) of 2.16. In terms of age, the mean age of the participants was 48.60 + -11.58 years, ranging from 28 to 72 years. Half of the patients were aged < 50 years old. There was a distinct cluster of patients aged 51–60 years, accounting for 36.84%

of the total sample, across both sexes. A significant proportion (84.21%) of patients came from urban areas, whereas a smaller proportion (15.79%) came from rural regions. The unemployed were the most numerous (26.32%), followed by farmers and civil servants (21.05%), and traders (18.42%). The majority of patients (39.47%) were married; 13 patients (34.21%) were widows (2.63%) or widowers (31.57%); and single and divorced represented 13.16% of the cases. Widowhood was associated with cardiovascular disease in HIV-infected patients, as indicated by statistical analysis (P=0.0171, $\chi 2$ =9.6611 for CI=95%). The majority of our patients were at the primary level (18 cases, 47.37%). The demographic information is summarized in Table 1.

Table 1: Socio demographic characteristics

Variables	Frequency(n=38)	Percentage		
	Age			
< or =30	2	5.26		
31-40	10	26.36		
41-50	7	18.42		
51-60	14	36.84		
61-70	3	7.89		
>70	2	5.26		
Mean age (+/-SD)	48.60+/-11	.58		
	Sex			
Male	12	31.58		
Female	26	64.42		
	Residence	•		
Urban	32	84.21		
Rural	6	15.79		
Marital status				
Single	5	13.16		
Married	15	39.47		
Divorced	5	13.16		
Widowed	13	34.21		
Study level				
No formal education	4	10.53		
Primary	18	47.37		
Secondary	13	34.21		
Tertiary	3	7.89		
Occupation				
Driver	1	2.63		
Trader	7	18.42		
Farmer	8	21.05		
Civil servant	8	21.05		
Retired	3	7.89		
Tailor	1	2.63		
No formal occupation	10	26.32		

3.2. Clinical characteristics

The primary symptom that drove the patients to seek medical attention was dyspnea in 21 cases (55.26% of the total cases). Chest pain, lower limb edema, cough, swelling, and painful leg were reported in 44.74%, 42.1%, 36.84%, and 34.21% of cases, respectively. In our study of right-sided heart failure, the peripheral physical signs of cardiac involvement varied among the patients. Lower limb edema was the predominant symptom, affecting 16 patients (42.11%). Painful hepatomegaly was another common finding, detected in 36.84% of the cases, followed by hepatojugular reflux in 34.21% of the patients. Notably, jugular vein turgescence was observed in 31.58% of the cases, while a positive Harzer sign and ascites were identified in 15.79% of the patients. Conversely, in our study, left-sided heart failure presented with a distinct set of symptoms. Dyspnea, experienced by 21

patients (55.26%), emerged as the most prevalent issue, followed by tachycardia, affecting 42.11% of the subjects. Additionally, cough was reported in 28.95% of the cases, with pulmonary stasis rales noted in 18.42% of individuals. Classifying the patients based on the NYHA stage, a larger proportion fell under stage III, encompassing 9 cases (42.86%), while the subsequent stage IV consisted of 8 cases (38.10%).

Moreover, thromboembolic disorders manifested uniquely in our study, with the primary indicator for deep vein thrombosis being a swollen and painful leg in all cases (100%), along with calf sloshing reduction noted in 92.31% of cases. Examining cases of cerebrovascular damage, three cases of stroke were recorded, constituting 7.89% of all cases. These strokes, which occurred in PLHIV patients at Kamenge Teaching Hospital during our study period, were characterized by symptoms such as fainting, aphasia, facial paralysis, and hemiplegia. Regarding HIV status, the largest proportion of patients affected by cardiovascular diseases was in stage III, with 23 cases (60.53%), whereas stage IV included 14 cases (36.84%), according to the revised classification of HIV/AIDS infection in 2016.

Table 2: Clinical characteristics

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3.3. Imaging findings

In a cohort of 23 patients who underwent chest radiography, the findings revealed that the majority, which accounted for 73.91% (17 patients), exhibited cardiomegaly. A subset of six cases (26.09%) displayed indications of pulmonary involvement, and the presence of unilateral or bilateral pleural effusion was reported in 13.04% of cases. X-rays returned normal results in four patients (17.40% of the total cases). Moving on to the electrocardiograms (ECGs) conducted on the cohort, the T-wave exhibited distinctive features, including normal in a significant proportion of cases (73.91%) and negative and symmetrical in approximately 21.74% of the cases. Sinus tachycardia emerged as the second most prevalent abnormality, affecting 12 patients (52.17%).

Shifting focus to the 24 cardiac ultrasounds done, results indicated that over half of the cases, precisely 54.17% (13 patients), featured dilation in one or more of the heart chambers. Moreover, hypokinesia and alterations in the left ventricular ejection fraction were observed in six cases, reflecting a prevalence of 25%. Doppler ultrasound has emerged as a pivotal diagnostic tool for assessing deep vein thrombosis (DVT) in the lower limbs. Thirteen patients exhibited lower limb DVT, with a significant proportion (53.85%) presenting with extensive DVT in this patient cohort. Furthermore, within the context of the study, 7.89% of the cases, which constituted three patients, experienced stroke. Specifically, the majority (66.67% or two-thirds of these stroke cases) were diagnosed as ischemic stroke.

	Chest X-ray	Frequency(n=23)	Percentage
Cardiomegaly		17	73.91
Pulmonary signs		6	26.09
Normal		4	17.39
Pleural effusion		3	13.04
	ECG findings	Frequency(n=23)	Percentage
ST segment	Normal appearance	20	86.96
	ST depression	3	13.04
T wave	Normal appearance	17	73.91
	Flat	1	4.35
	Symmetric T wave inversion	5	21.74
	Sinus tachycardia	12	52.17
Le	eft bundle branch bloc	9	39.13
Left	Ventricular hypertrophy	9	39.13
Lov	v voltage QRS complex	4	17.39
L	eft atrial hypertrophy	4	17.39
Ri	ght atrial hypertrophy	2	8.69
Right bundle branch bloc		1	4.35
Ventricular extrasystole		1	4.35
1	Atrioventricular bloc	1	435
Normal		1	4.35
Echo	cardiographic findings	Frequency(n=24)	Percentage
Dilated heart chamber		13	54.17
Hypokinesia		6	25
Altered Ejection Fraction		6	25
Insufficient or stenosed valve		5	20.83
Pericardial effusion		5	20.83
Hypertrophic wall		3	12.50
Normal		2	8.33
Hyperkinesia		1	4.17
Location of deep vein thrombosis		Frequency(n=13)	Percentage
Distal deep vein thrombosis		5	38.46
Extensive deep vein thrombosis		7	53.85
Proximal deep vein thrombosis		1	7.69
Cer	ebral CT scan findings	Frequency(n=3)	Percentage
	Hemorrhagic stroke	1	33.33
Ischemic stroke		2	66.67

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3.4. Laboratory findings

In our study, anemia was present in a significant percentage of patients (52.63%). This was the most common hematological abnormality observed in the present study. Lymphopenia was identified in 11 cases, accounting for 28.95% of the total cases, followed by thrombocytosis seen in 8 cases, making up 21.05% of the study group. Furthermore, we noted that kidney function was impaired in a significant proportion of cases, totaling 34.21% of the study group. Chronic kidney disease was found to be closely associated with anemia (p=0.0044; $\chi 2 = 8.1080$; IC=95%). Moreover, when analyzing 18 samples sent to the laboratory to detect acid alcohol-resistant bacilli, we discovered their presence in 44.44% of the patients tested.

3.5. Prevalence of cardiovascular diseases

In our comprehensive study of cardiovascular diseases in

HIV-infected patients, deep vein thrombosis (DVT) emerged as the predominant condition, accounting for 34.21% of cases. Dilated cardiomyopathy was the second most prevalent disease (28.95%). We also observed considerable presence of valvular heart disease (21.05%), ischemic heart disease (18.42%), hypertension (15.79%), pericarditis (13.16%), and stroke and pulmonary arterial hypertension (7.89%). Furthermore, pulmonary embolism, and arrhythmia-induced cardiomyopathy were present in 2.63% of our patients. In addition to these cardiovascular diseases, our investigation revealed a range of comorbidities among the individuals studied. Chronic kidney disease, digestive candidiasis, tuberculosis, asthma, Kaposi sarcoma, gout, and hepatitis C were reported in 34.21%, 26.32%, 23.68%, 7.89%, 7.89%, 5.26%, 5.26% respectively.

Table 4: Prevalence of cardiovascular diseases

Diagnosis	Frequency(n=38)	Percentage
Deep vein thrombosis	13	34.21
Dilated Cardiomyopathy	11	28.95
Valvular cardiopathy	8	21.05
Ischemic cardiomyopathy	7	18.42
Hypertension	6	15.79
Pericarditis	5	13.16
Stroke	3	7.89
Pulmonary arterial hypertension	3	7.89

Hypertrophic cardiomyopathy	3	7.89
Chronic cor pulmonale	1	2.63
Pulmonary embolism	1	2.63
Arrhythmia-induced cardiomyopathy	1	2.63

4. Discussion

The study included 115 HIV patients, with 38 meeting the inclusion criteria, making up 33.04% of the sample with 26 females (68.42%) and 12 males (31.58%), resulting in a sex ratio (Women/Men) of 2.16. An analysis of large North American and European cohorts found that women with HIV have an elevated risk of CVD compared to men with HIV of the same age ^[17]. Women with HIV have a higher risk of CVD, including myocardial infarction and stroke, than men ^[18]. Possible explanations for these findings include sex hormone synthesis [19], increased systemic inflammation, and immunological activation that affects vascular function ^[20]. In our study, the mean patient age was 48.60 ± -11.58 years. Many studies found that cardiovascular diseases occur at young age in HIV-infected patients ^[21]. The unemployed were the most numerous (26.32%), followed by farmers, civil servants, and traders (21.05 %, 21.05 %, and 18.42 %, respectively). Research indicates a positive correlation between work position and HIV testing, care access, and medication adherence ^[22]. Unemployment is linked to decreased HIV testing, delayed diagnosis [23], late access, and low adherence to highly active antiretroviral therapy [24]. This may explain the large number of unemployed patients in our study. The majority of the patients were married (39.47%), followed by widowers (31.57%). In our study, widowhood was associated with cardiovascular disease (p = 0.0171, $\chi 2 =$ 9.6611 for CI = 95 %). Single/non-cohabiting women face numerous risk variables that could have a significant impact on the trajectory of the epidemic ^[25]. The majority of affected patients were at the primary level (47.37%), possibly because of a lack of information on HIV/AIDS and its consequences. The study found that patients with cardiovascular disease often present with a variety of symptoms, leading to their visits to healthcare providers. Dyspnea was the primary symptom (55.26%), followed by chest pain (44.74%), lower limb edema (42.1%), cough (36.84%), and swelling and leg pain (34.21%). This suggests the need for thorough evaluation by healthcare professionals to provide accurate diagnosis and appropriate management strategies. Left-sided heart failure has a distinct set of symptoms, with dyspnea being the most prevalent. A larger proportion of patients were classified as stage III (42.86%) or IV (38.10%) according to the NYHA classification. HIV status also affects the majority of patients with cardiovascular disease. Lower limb edema was the predominant symptom, affecting 16 patients (42.11%) in the cohort with right-sided heart failure. Concerning HIV status, the largest proportion of patients affected by cardiovascular diseases were in stage III, 23 patients (60.53%), whereas stage IV encompassed 14 patients (36.84%), as per the classification of HIV/AIDS infection in 2016 while stage I or II were represented in 78% in the study conducted in Malawi^[26].

In this study, 23 patients with PLHIV who underwent chest X-rays, the findings revealed that 73.91% of them had cardiomegaly, with pulmonary involvement (26.09%) and pleural effusion (13.04%) being common. The study also found that electrocardiograms (ECGs) were abnormal in 73.91% of cases, with sinus tachycardia being the most prevalent abnormality in 52.17% of the cases. Cardiac

ultrasounds revealed dilation in one or more heart chambers in 54.17% of cases, with hypokinesia and alterations in left ventricular ejection fraction in 6 cases (25%). Doppler ultrasound was the pivotal diagnostic tool for deep vein thrombosis in the lower limbs in 34.21% of cases. A total of 3 cases of stroke were recorded, involving ischemic stroke (66.7%), which is more common than hemorrhagic strokes in cases during HIV ^[27]. The studies suggest that HIV infection should be included in the diagnosis of young stroke patients ^[28].

In our study, anemia was found in 52.63% of cases of HIVinfected individuals in our study, followed by lymphopenia in 11 cases (28.95%), thrombocytosis in 8 cases (21.05%), hyperleukocytosis and leukopenia in 2 cases (5.26%) each, and pancytopenia in one case (2.63%). Kidney function was impaired in 34.21% of cases, with chronic kidney disease being closely associated with anemia ((statistically significant as indicated by p=0.0044, with a χ 2 value of 8.1080; IC: 95%). Renal illness affects 6-48.5% of HIVinfected individuals in Africa^[13], with classic HIV-associated nephropathy in South Africa^[29].

The study found that deep vein thrombosis (DVT) was the most prevalent cardiovascular disease, accounting for 34.21% of cases. Dilated cardiomyopathy was the second most prevalent at 28.95%, followed by valvular heart disease at 21.05%, ischemic heart disease at 18.42%, hypertension at 15.79%, pericarditis at 13.16% and stroke, pulmonary arterial hypertension, hypertrophic cardiomyopathy at 2.63% each. A study in Soweto, South Africa, found that HIV-related cardiomyopathy was the most common initial diagnosis (38%), followed by pericarditis or pericardial effusion (25%) [³⁰].

Comorbidities such as chronic kidney disease, digestive candidiasis, and tuberculosis were also identified at 34.21%, 26.32%, 23.68% respectively, emphasizing the need for attention in managing cardiovascular diseases. Tuberculous pericarditis should always be considered in the face of a clinical picture of tuberculosis in PLHIV in our region where tuberculosis is a most frequent opportunistic infection during HIV infection, especially in the advanced stage of the disease. Other conditions like asthma and Kaposi sarcoma were also observed, highlighting the complexities of managing multiple health concerns in HIV patients.

5. Limitations of the study

At the end of this study, we received results that were compared to the most recent literature. Our study suffers from certain shortcomings, in particular the reduced number of patients treated during the study period who presented with at least one cardiovascular disease, in addition to the imprecision in the etiological diagnosis of cardiac damage (opportunistic infection or neoplasia, role of nutritional disorders, anemia, specific involvement of the HIV), lack of financial or technical means for explorations, delays in HIV testing leading to potential inaccuracies.

6. Conclusion

Cardiovascular diseases in HIV-infected patients are many and varied. The most common were deep vein thrombosis of the lower limbs followed by dilated cardiomyopathy, valvular, ischemic and hypertensive heart disease responsible for heart failure in young people with profound immunosuppression. Other types of cardiovascular disease accounted for less than 10% of cases. The majority of patients who were the subject of our study were at WHO clinical stage III according to the classification of HIV infection revised in 2016 followed by stage IV.

7. Ethical consideration

The ethics committee of Kamenge Teaching Hospital authorized the project. This study was conducted in accordance with the Declaration of Helsinki. All participants provided signed informed consent. Prior procedures have already been undertaken to protect participants' identities and information, ensuring complete anonymity and secrecy.

Authors' contribution

All authors made significant contributions to each of the following:

Dionys Nsanzabagenzi: conception and design of the study, drafting the manuscript, writing the final version. Epipode Ntawuyamara: Data collection, drafting the manuscript. Pengfei Ye: Data analysis and interpretation. Hongxin Niu: Supervision, writing and critically reviewing the article for key intellectual substance, follow publication process. All authors approved the final manuscript to be submitted.

Disclosure of interest

The authors declare that they have no competing interest.

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