

# Risk Factors for Stroke Associated with HIV at Loandjili General Hospital in Pointe-Noire (Congo)

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**Abstract:** Introduction: HIV infection and stroke constitute a major public health problem due to their morbidity and mortality. In people living with HIV the risk of developing a stroke is high. Objective: To establish the causal link between HIV and the onset of stroke in order to determine the risk factors for stroke associated with HIV at loandjili general hospital. Patients and Methods: It was a case-control study, prospective from January to July 2019, carried out in the department of Pointe-Noire, including any patient hospitalized for stroke confirmed by brain scan, any patient hospitalized or coming for an outpatient consultation. pathologies unrelated to stroke. The statistical analysis was carried out using the EPI info 7.2 software. Results: Two hundred patients were included in our study, including 100 cases and 100 controls. The relative frequency of HIV was 17% in cases versus 43% in controls. Young age was the risk factor for stroke associated with HIV. This risk factor was potentiated by immunosuppression of CD4 + T lymphocytes. Seventy-eight (78%) of stroke + / HIV + patients had a CD4 + count <200 / mm<sup>3</sup>. DALY was the predominant mechanism of injury with a frequency of 56% in people living with HIV. Conclusion: Stroke-HIV co-morbidity is frequent in Pointe-Noire. The risk factors for stroke / HIV + are dominated by young age. However, our study did not show a causal link between HIV and the onset of stroke.

**Keywords:** Stroke, HIV, Case-controls, Pointe Noire, Congo

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## 1. Introduction

Stroke and HIV infection are two major global public health problems. In Africa, the prevalence of stroke is between 5 and 24% [1]. OSSOU NGUIET et al [2] noted that stroke is the first vascular emergency at the CHUB and the main cause of death in the neurology department. Likewise, Thierry GOMBET et al [3] reported a frequency of ischemic strokes (DALYs) of around 3.4% in the emergency room. Stroke morbidity and mortality are partly linked to the HIV pandemic as evidenced by the high frequency of stroke and HIV co-morbidity. Epidemiological studies on stroke in PLHIV, although controversial, suggest that

stroke is associated with a profile of cardiovascular risk factors that would be different in subjects without HIV infection [4-6]. A recent study in the department of Pointe Noire noted a profile of different risk factors in people living with HIV [7].

It is in this context that we wanted to establish the causal link between HIV and the occurrence of stroke in order to determine the risk factors for stroke associated with HIV at Loandjili general hospital.

## 2. Patient and Method

This was a prospective case-control study, from January 1

to July 31, 2016, a period of 7 months, carried out in the Neurology Department of Loandjili General Hospital.

Depending on the issue of our study:

The case group was defined as all patients with stroke confirmed by a brain scan.

The test group was defined as all patients who had not had a stroke and had no known RDF until the day of the outpatient.

The positivity of VRS was our study variable of interest considered as an exposure factor at the origin of the present case-control study.

Have been included:

Group of patients constituting the group of cases:

Was selected, any patient admitted to the neurology department with a stroke confirmed by a brain scan.

Group of non-patients constituting the group of witnesses:

Any patient admitted to the neurology outpatient department for pathologies unrelated to neuro-vascular pathologies was selected.

In both groups, final inclusion was made after informed

consent.

The variables studied were: age, sex, vascular risk factors, HIV test results, and type of stroke.

The database was made from the 2010 version of Microsoft Excel. Qualitative variables were expressed as frequency and quantitative variables as mean $\pm$ standard deviation. Fisher's Chi2 Exact test was used for univariate analysis between two variables.

### 3. Results

Our study included 200 patients meeting the inclusion criteria including 100 cases and 100 controls.

The case group has a mean age of  $56.92\pm 11.21$  with extremes ranging from 30 to 86 years.

The mean age of the control group was  $43.3\pm 14.3$  with extremes ranging from 20 to 82.

Figure 1 shows the distribution of the case study and control population by age group.

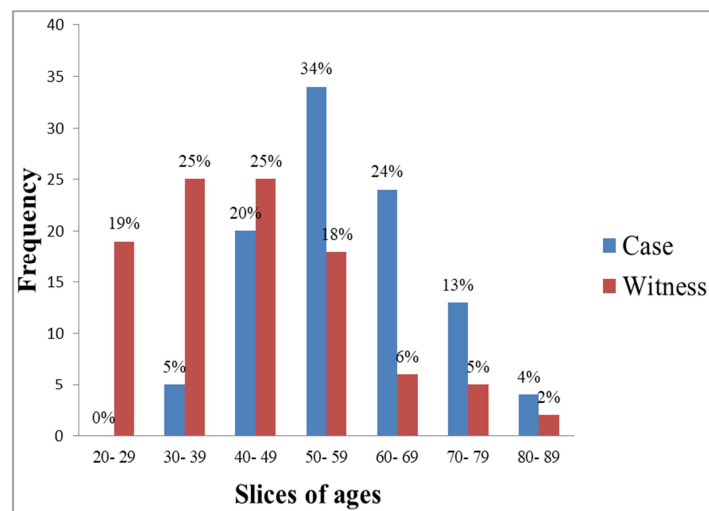


Figure 1. Distribution of the study population (cases and controls) according to age.

Figure 2 depicts the distribution of cases and controls by gender.

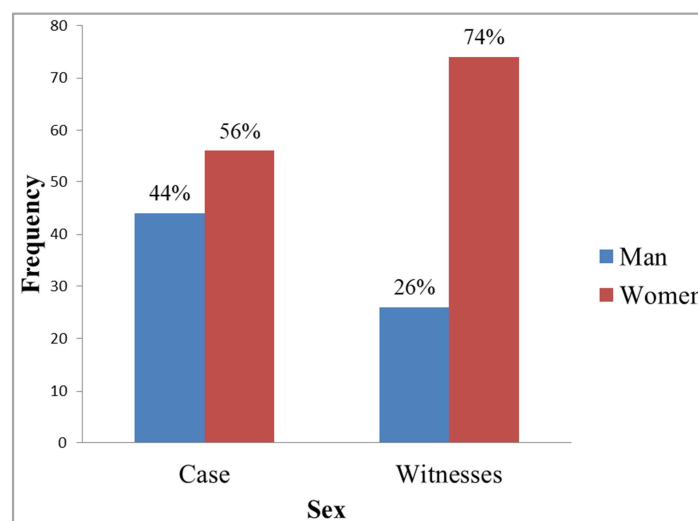


Figure 2. Distribution of case and control groups according to sex.

Women were more represented in the two groups with an M / F sex ratio=0.78 in the cases and a M / F sex ratio=0.35 in the controls.

Table 1 describes the distribution of the study population according to stroke risk factors.

*Table 1. Stroke risk factors in the Patient and Control groups.*

Stroke risk factors	Case		Witnesses		Total	
	N	%	N	%	N	%
HTA						
Yes	83	83	13	13	96	48
No	17	17	87	87	104	52
Tobacco						
Yes	2	2	1	1	3	1,5
No	98	98	99	99	197	98,5
Diabetes						
Yes	10	10	3	3	13	6,5
No	90	90	97	97	187	93,5
Alcohol						
Yes	12	12	11	11	23	11,5
No	88	88	89	89	177	88,5
Obesity						
Yes	8	8	1	1	9	4,5
No	92	92	99	99	191	95,5

Table 2 shows the HIV serological status (exposure factor of interest) studied in the cases and in the controls.

*Table 2. HIV serological status in the study population.*

Serology	Case		Whitesses		Total	
	N	%	N	%	N	%
HIV+	17	17	43	43	60	30
HIV-	83	83	57	57	140	70
Total	100	100	100	100	200	100

Univariate analysis (Table 3).

*Table 3. Univariate analysis of the different variables.*

Variables	Case	Witnesses	OR	IC95%	P
Age*	56,9±0,5	43,3±14,3	6,7	(3,6-12,4)	0,0000
Femal sex†	56	74	2,2	(1,2-4,1)	0,008
Risk factors					
Diabetes†	10	3	3,6	(1-13,5)	0,06
Obesity†	8	1	8,6	(1,1-69,8)	0,04
HTA†	83	13	32,6	(14,9-71,3)	0,0000
Alcoholism†	12	11	1,1	(0,5-2,6)	0,8
Smoking†	2	1	2,1	(0,1-22,6)	0,56
SRV					
HIV+	17	43	0,3	(0,1-0,5)	0,0001
HIV-	83	57			

\* Average±standard deviation

† Percentage (%)

Table 4 represents the multivariate analysis of the different variables.

*Table 4. Multivariate analysis of the different variables.*

Variables	Case	Witnesses	ORA	IC 95%	P
Age*	56,92±11,21	43,3±14,3	1,05	(1,02- 1,08)	0,02
Femal sex†	56	74	2,51	(0,99- 6,39)	0,05
HTA†	83	13	24,56	(10,16- 59,34)	0,00
Obesity†	8	1	2,14	(0,22- 20,88)	0,58
HIV†	17	43	0,43	(0,16- 1,14)	0,09

ORA: Adjusted odds ratio

\* Average±standard deviation

† Percentage (%)

Table 5 illustrates the distribution of patients with stroke according to the type of stroke.

**Table 5.** Distribution of stroke patients according to the type of stroke.

Strok	Case HIV+		Case HIV-		Total	
	N	%	N	%	N	%
Hemorrhagic stroke	8	47,06	36	43,37	44	44
Ischemic stroke	9	52,94	47	56,63	56	56

P=0.79

Table 6 shows the distribution of the CD4 T lymphocyte count according to the type of stroke.

**Table 6.** Distribution of the CD4 T lymphocyte count according to the type of stroke.

Number of CD4+	Ischemic stroke		Hemorrhagic stroke		Total	
	N	%	N	%	N	%
< 200	7	78	3	43	10	63
≥ 200	2	22	4	57	6	37
Total	9	100	7	100	16	100

P value=0.30.

## 4. Discussion

The relative frequency of HIV infection was 17% in the stroke group versus 43% in the control group. Our results corroborate most of the studies in the literature. Indeed, the studies of Koumeka [7] in Congo, Qureshi et al [5], in Malawi, Gnonlonfoun et al [8], in Benin, Heikinheimo et al [9], in Malawi, respectively reported prevalences of 1 HIV infection in the order of 20%, 22%, 26.1% and 34% in stroke patients. The high frequency of HIV infection observed in the group of patients in our study could be explained by: i) the advanced age of stroke patients (57.4±11.2 years) which would explain a greater risk of Stroke following loss of vascular elasticity combined with immunosuppression due to HIV; ii) the stroke would indeed be the consequence of an immunocompromised field at an advanced stage of HIV infection. A few authors have reported that HIV infection is a contributing factor in around 25% of stroke cases in Africa. The pathophysiology of HIV infection is in favor of chronic inflammation by increasing the risk of vasculitis, thrombi and various abnormalities predisposing to hypercoagulation [10-12]; iii) Finally, the difference observed between different studies and ours may be due to the sensitivity of the tests used and the methodology applied.

In our study, we noted a more or less balanced distribution in the case group and a predominance of the female sex in the controls. However, the comparison of the two groups showed a significant difference for the female sex.

Although the female predominance in the occurrence of stroke was noted in a study conducted in Côte d'Ivoire [13] with a sex ratio of 1.2, most of the work on strokes in PLWHIV found a male predominance [8, 9, 14, 15]. In fact, Longo-mbenza et al [14], reported a male predominance with a frequency of 94.1% in PLHIV victims of stroke. This frequency was higher than ours. Gnonlonfoun et al [8] reported a male sex frequency of 51.3%.

The age group most represented in patients was that ≤ 59

years old with 59 patients and the difference observed was significant. The prevalence of stroke in people in their 40s / 50s can be explained by the high prevalence of HIV and other sexually transmitted infections in this age group in Congo [4]. This is the sexually active age group as pointed out by Gnonlonfoun et al [8] and Sen et al [4].

The frequency of hypertension in patients in our study was 83% versus 13% in controls. The high frequency of hypertension during stroke has been reported in several studies in Congo [2, 16]. Compared to controls, the difference was statistically significant. The study by Connor et al [10] found a frequency of hypertension of 55% in PLHIV. Longo-mbenza et al [14], report a frequency of hypertension greater than 100%. Gnonlonfoun et al [8], on the other hand, noted a frequency of hypertension of 32.7% in stroke / HIV + patients lower than that reported in our study. Tipping et al [6] reported an even lower frequency of hypertension of 10%. The difference in the prevalence of hypertension, observed in the different studies, could be explained by the size of the study sample, the choice of the study population (young subjects exclusively), and the methodology of the study. Either way, hypertension is the major risk factor for stroke in the world. Our results are therefore in line with the literature as shown by the study by Kimbally-Kaky et al [17] who report that hypertension is the main cardiovascular risk factor in Congo.

In our study, we reported the relative frequency of smoking to 1% in cases and controls, respectively. The observed difference was not statistically significant (p value=1).

The smoking prevalence reported in our case study (1%) was significantly lower than that reported by Gnonlonfoun et al [8], Chow et al [18], Marcus et al [19] and Ortiz et al [20], in stroke / HIV + patients, respectively 18.6%, 48%, 45.2%, and 50% with a very significant difference. This difference in smoking prevalence, reported by different studies in stroke / HIV + patients, could be explained by the different lifestyle of the populations studied. Smoking is one of the main

vascular risk factors in industrialized countries.

We reported a frequency of alcoholism at 12% and 11% respectively in cases and controls. The observed difference was not statistically significant ( $p$  value equals 1). Our results are close to those of Marcus *et al* [19], who reported a prevalence of alcoholism of 11.2%. Tipping *et al* [6] report a prevalence of alcoholism at 28% in stroke / HIV + patients versus 25% in stroke / HIV- patients [8], with no significant difference. However, Longo-mbenza *et al* [24] reported a prevalence of alcoholism of 94.1% with a statistically significant difference. Alcoholic habits could be at the base of the observed differences.

In our study, the relative frequency of DST2 was 10% and 3% in cases and controls, respectively. The observed difference was not statistically significant with a  $P$  value=0.08.

Our results are close to those reported by Gnonlonfoun *et al* [8], who noted a prevalence of diabetes mellitus of 11.5% in stroke / HIV + patients, without significant difference, Gutierrez *et al* [21], who reported at 11, 5% the prevalence of diabetes mellitus in stroke / HIV + patients with a statistically significant difference ( $p$  value <0.001). However, Chow *et al* [22] reported the prevalence of diabetes mellitus in stroke / HIV + patients at 22%, with a statistically significant difference ( $p$  value <0.001). The differences observed could be explained by the choice of study methodology. The inclusion of PLHIV treated with antiretrovirals by Chow *et al* [22] and Gutierrez *et al* [21] could explain the higher prevalence of diabetes mellitus in stroke / HIV + patients with a significant difference. Several studies have proven the risk of metabolic disorders occurring in patients treated with anti-retrovirals (ARVs), in particular protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) leading to metabolic syndrome and insulin -resistance, making the bed of diabetes mellitus [23, 25].

In our study, we did not include PLHIV on ART. The role of HIV itself was proven in the development of metabolic syndrome in PLHIV in the SMART study [26].

All of these results show that diabetes is a risk factor for stroke in people living with HIV. In order to reduce the morbidity associated with diabetes mellitus in PLWHIV, systematic screening for diabetes mellitus and glycemic control should be optimized.

We noted the frequency of obesity to be 8% in cases versus 1% in controls. The observed difference was significant with a  $P$  value equal to 0.03. Adjedje [27] reports an obesity frequency of 33.3%, higher than ours. The high frequency of android obesity could be explained by the metabolic syndrome induced by HIV. However, weight loss in the African and Congolese context in particular is badly experienced by the patient because it is often a source of stigmatization especially among PLWHIV, which justifies that the subjects prefer to be obese.

Obesity is a modifiable, intermediate cardiovascular risk factor [28]. It contributes, in the more or less long term, to the increase in blood pressure levels by increasing the overall blood volume, without increasing peripheral resistance [29]. In association with hypertension, diabetes mellitus,

hypoHDL-cholesterolemia and hypertriglyceridemia. It constitutes one of the elements defining the metabolic syndrome [30].

Weight reduction implies a significant reduction in blood pressure in the absence of a low-sodium diet [15].

The multivariate study of the known RDFs of stroke and HIV as an exposure factor for stroke in a case-control study model showed that HIV was not an independent risk factor for stroke in stroke / HIV + patients compared to stroke / HIV- patients. The odds ratio of HIV (0.43; 95% CI: 0.16-1.14) adjusted for other statistically significant risk factors (age sex, hypertension, obesity, triglycerides) made it possible to note that HIV is not a main factor in the onset of stroke. However, several studies in the literature have shown that HIV infection increases the risk of stroke [8, 9, 24]. However, the mechanisms of this stroke / HIV relationship remain multifactorial and have yet to be defined.

## 5. Conclusion

HIV seroprevalence in patients victims of stroke, at Pointe-Noire (17%) is high. The risk factors of the AVC / HIV + association are mainly dominated by young age, which can be explained by the high prevalence of HIV and other sexually transmitted infections in this age group. Risk factors are dominated by arterial hypertension, tobacco, alcohol and diabetes. However, our study does not report an association between the different risk factors and the immunodepression of TCD4 + lymphocytes.

## Conflict of Interest

The authors declare that they have no competing interests.

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