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Cerebral alterations in West African HIV and non-HIV adults aged ≥50: An MRI study

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Abstract

Objectives: To cross-sectionally describe brain alterations in PLHIV aged above 50 years old, receiving antiretroviral treatment (ART) and living in Senegal compared to HIV-negative subjects.

Methods: Twenty PLHIV and 26 HIV-negative subjects with comparable socio-demographic and clinical characteristics underwent an MRI exam (3D-T1 and FLAIR sequences). Global atrophy and White Matter Hyperintensities (WMH) were evaluated. After assessing the feasibility and acceptability of MRI scans in this population, we described atrophy and WHM prevalence and associated factors using logistic regressions.

Results: Overall, 43.5% of the study sample were aged ≥60 years, 58.7% were women, and 28.3% had hypertension. The overall prevalence of atrophy and WMH was 19.6% [95% CI: 8.1–31.1] and 30.4% [95% CI: 17.1–43.7]. HIV status had no significant effect on atrophy or WMH. Unemployment and hypertension were significantly associated with atrophy, whereas women were less likely to present atrophy. Aged ≥60 years was the only factor associated with WMH.

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Conflict of interest

The authors have no conflict of interest to declare.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2020.12.016.

Conclusions: A high prevalence of atrophy and WMH was observed in West African adults aged over 50 years without a clear HIV impact. As brain MRI studies are critical to better understand cognitive and emotional outcomes, we encourage those studies in older PLHIV in West Africa.

Keywords

HIV; Aging; Brain; MRI; West Africa

Introduction

HIV associated neurocognitive disorders (HAND) (Antinori et al., 2007) have long been described with harmful consequences for daily life and HIV-related outcomes (adherence to treatment, AIDS occurrence, mortality) (van Gorp et al., 1999; Hinkin et al., 2004; Kordovski et al., 2017; Rusch et al., 2004; Tozzi et al., 2005). Despite Antiretroviral Therapy (ART) initiation, HAND prevalence remains high in western countries (Bonnet et al., 2013; Valcour, 2013). In Sub-Saharan Africa (SSA), the pooled prevalence of cognitive impairment was estimated in a recent meta-analysis at 30.9% among people living with HIV (PLHIV) on ART (Habib et al., 2013). Neurocognitive disorders can also be aggravated by age-related cognitive decline. According to recent UNAIDS estimates, the number of PLHIV aged ≥50 years worldwide has been increasing since 1995 (UNIAIDS, n.d.). SSA is the world region the most affected by this trend, with the highest number of PLHIV aged ≥50 years (in 2019, 4.4 millions) (UNIAIDS, n.d.). As the care programs specialized in HIV infection are unprepared to deal with such an aging population (Mills et al., 2012; Negin et al., 2012), in-depth description and understanding of the cerebral alterations that could occur in this population are needed. Neuroimaging techniques, particularly Magnetic Resonance Imaging (MRI) as a non-invasive method, are widely used to describe brain changes and understand the physiopathology of HIV-related cerebral alterations in western countries.

MRI studies of PLHIV on ART reported that in addition to age-related grey matter changes, atrophy related to HIV-infection occurs in subcortical regions (Ances et al., 2012) and in the neocortex (Becker et al., 2011; Holt et al., 2012; Towgood et al., 2012). In the Comorbidity in Relation to AIDS (COBRA) project conducted in the United Kingdom and the Netherlands, it was reported lower grey matter volumes in PLHIV on ART than in HIV-negative subjects (van Zoest et al., 2018) with no higher rates of changes after two years of follow-up (Cole et al., 2018). These alterations have been linked to cognitive disorders (Becker et al., 2011). To date, no specific description of atrophy in older PLHIV is available in SSA. Two published MRI studies were conducted in South Africa, but in middle-aged adults and focusing on the HIV subtype C impact (predominant in this region of the world) (Heaps et al., 2012; Ortega et al., 2013).

White matter hyperintensities (WMH), considered as ischemic lesions and radiological markers of cardiovascular disease of small vessels (DeCarli et al., 2005; Jeerakathil et al., 2004), are also commonly observed in PLHIV living in western countries (McDonnell et al., 2014; McMurtray et al., 2008; Su et al., 2016). An increased burden of WMH has also been associated with cognitive deficits in PLHIV (Su et al., 2016), suggesting that vascular

pathology may be a significant factor in developing cognitive impairment in PLHIV (Brew, 2016).

Due to the more widespread use of antiretroviral drugs with primary mitochondrial toxicity and different exposure to SSA risk factors, these brain-change characteristics might be different from those observed in western countries. In this context, after assessing the feasibility and acceptability of a brain MRI study in Senegal, we aimed to evaluate (1) the prevalence of atrophy and WMH in PLHIV aged above 50 years old and living in this country in comparison to HIV-negative subjects, (2) factors associated with atrophy and WMH in this population.

Methods

Ethical consideration

Ethical clearance was obtained from Senegal's national ethics committee (Conseil National d'Ethique de la Recherche en Santé (CNERS)). The study's purpose was fully explained to all participants who gave their written consent before being included in the study. Participants' right to refuse the participation was kept, and the confidentiality of the participants was guaranteed.

Participants

All participants lived in Dakar, Senegal. The inclusion period of this cross-sectional study occurred from October 2018 to June 2019. PLHIV were recruited at the time of their 2-year follow-up visit in the NeuroAging study (N = 39). The NeuroAging study is a longitudinal multicenter cohort designed to evaluate cognitive impairment, physical function, and depression in PLHIV aged 50 years old and above, living in West Africa (Senegal, Côte d'Ivoire). This is an ancillary study embedded within the West Africa network of the International epidemiological Databases to Evaluate AIDS (IeDEA) of the US National Institutes of Health (https://www.iedea.org/regions/west-africa/) (Egger et al., 2012). The inclusion criteria in the NeuroAging study were type-1 HIV, being aged 50 years old or older, and on ART for at least six months.

HIV-negative subjects were recruited as healthy controls in the same hospital at the time of their inclusion in the NeuroAging study (included as a comparison group for cognitive evaluation). They were recruited from subjects aged 50 or over, with an HIV-negative serology less than 15 days and who came for voluntary screening for HIV infection in three sites: the Regional Center for Research and Training in Clinical Management (CRCF), the infectious and tropical disease department, the Ambulatory Treatment Center (CTA) or the blood transfusion center at Fann National University Hospital in Dakar, Senegal. In the present study, they were selected to have similar socio-demographic characteristics to the included PLHIV.

For all participants, the exclusion criteria were as follows: 1/ contraindications to MRI, 2/ major acquisition artifacts on MRI data, and exclusion criteria specific to the NeuroAging study: neurological pathology (history of stroke or Parkinson's disease), psychiatric illness (including psychotropic treatment), impaired vision preventing good ability to take cognitive

tests and specifically for patients: having a history of opportunistic cerebral infection, a current disabling opportunistic infection, meningitis, a sensory-motor paralysis, or cancer under treatment or a respiratory or cardiac insufficiency (a part of the study concerned physical function).

MRI acquisition

MRI examination was performed using a 1.5T Magnetom Avanto (Siemens) in the radiology service at the Principal Hospital in Dakar, Senegal. Anatomical high-resolution MRI volumes were acquired using a 3D MPRAGE T1-weighted sequence with the following parameters: TR = 2700 ms, TE = 3.54 ms, TI = 1000 ms, 7-degree flip angle, FOV = $256 \times 256 \times 192$ mm^3 to cover the whole brain, with a voxel size of $1 \times 1 \times 1$ mm^3, no gap. To describe WMH, we also used a 2D FLuid-Attenuated Inversion Recovery (FLAIR) T2-weighted sequence with the following parameters: TR = 11850 ms, TE = 98 ms, TI = 2500 ms, FOV = 230×230 mm^2, with 52 slices of 3 mm thickness, yielding a voxel size of $0.9 \times 0.9 \times 3$ mm^3, no gap.

Data collection

Participants' socio-demographic characteristics as age, gender, education level, marital status, and professional activity were recorded. During the inclusion visit, participants were also asked if they had ever been diagnosed with these comorbidities: hypertension, diabetes, hyperlipidemia, C or B hepatitis, tuberculosis, migraine. For the PLHIV, this information could be completed with the patients' medical history. History of trauma or neurologic diseases was also documented. Tobacco and drug substance use (i.e., current, former, or never) was evaluated through basic questions. Hazardous alcohol drinking was also described using AUDIT-C (score ≥4 for men or ≥3 for women). The presence of severe depressive symptoms was considered positive with a total score of ≥17 for men and ≥23 for women, using the Center for Epidemiological Studies Depression scale (CES-D) (Fuhrer and Rouillon, 1989).

For PLHIV, specific data were collected to document their initial clinical stage (defined using the Centers for Disease Control and Prevention (CDC) definition (A, B or C)), their CD4 Nadir, and their more recent CD4 presented in two categories (≤200 vs. >200 cells/µl and <500 vs. ≥500 cells/µl, respectively). The duration of HIV disease was also calculated as the delay in months between the first positive serology date and the study's inclusion date. Exposure to zidovudine (AZT), didanosine (ddI), stavudine (D4T) in the initial ART treatment, and also in the current ART treatment was studied through a categorical variable (yes/no).

Outcomes

Feasibility and acceptability—The study's feasibility was evaluated using two indicators: the delay between inclusion and MRI and the access to the machine. The acceptability was evaluated using the refusal rate. The satisfaction of the participants was also assessed but just orally.

Global brain volumes and White Matter Hyperintensities volumes—Global brain volumes and White Matter Hyperintensities volumes were computed using volBrain and LesionBrain, respectively. VolBrain (Manjón and Coupé, 2016) and LesionBrain (Coupé et al., 2018) are two free online MRI brain volumetry system, allowing easy access to a fully automated segmentation of the three brain compartments (GM, WM, and Cerebro Spinal Fluid) and WMH, respectively (see more technical information in supplementary data). Total Intracranial Volume (TIV) was calculated by adding volumes of the three brain compartments. Here, we focused on global GM, WM, and brain parenchyma (GM + WM) volumes and total, periventricular, and deep WMH volumes. Each volume was normalized (i.e., using TIV) for the following analyses.

Global atrophy and white matter hyperintensities (qualitative evaluation)—Global atrophy was assessed using the Koedam score (Koedam et al., 2011), a 4-level score (0 to 3), the fourth level corresponding to the most extensive atrophy. This scale is usually used by neuroradiologists in Dakar, Senegal. We also evaluated the presence of white matter hyperintensities (WMH), according to the STRIVE criteria (Wardlaw et al., 2013) combined with the modified Fazekas scale (Fazekas et al., 1987; Inzitari et al., 2009). This is a 4-level scale (0 to 3), the fourth level corresponding to a high WMH burden. Due to the small sample size, the scores were recoded as a binary variable (absence (scores 0 to 1) vs. presence (score 2 to 3)). Global atrophy and the presence of WMH were evaluated by two trained investigators (A.N.D. and C.B.).

Statistical analysis

The study sample's characteristics were described using numbers and proportions for categorical variables for each group and were compared using the Fisher exact test. Global and WMH volumes were presented with the median and interquartile quartile for normalized volumes (%). They were compared using the Wilcoxon rank-sum test. The prevalence of atrophy and WMH burden and the confidence interval at 95% were reported in the whole sample and for each group.

We evaluated, in the whole sample, factors associated with (1) atrophy and (2) severe WMH, using univariate and multivariate logistic regression analyses. The multivariable logistic regression models included all variables associated with the dependent variable with a p-value of ≤ 0.25 in univariate analyses. Unbalanced variables (85%/15%) were excluded from the analyses. In the final model, obtained with a backward selection, we considered significant associations at $p < 0.05$. In the model, factors associated with atrophy, age, and educational level were considered confounding factors. The Goodness of Fit (GoF) of the final model was evaluated with the Hosmer-Lemeshow test ($p > 0.05$). The effect sizes were also computed using the V de Cramer.

Additionally, in PLHIV only, using Wilcoxon tests for continuous variables or using Fisher exact tests for categorical variables, we evaluated the association between atrophy and WMH and HIV outcomes.

Finally, the associations between atrophy or severe WMH and cognitive performance were also assessed using Wilcoxon tests. As no significant HIV status effect was observed on the

presence of atrophy or severe WMH, we decided to explore these associations in the whole sample.

A multivariable imputation of missing data was performed with a Random Forest procedure.

Statistical analyses were computed using the SAS software 9.4 version.

Results

Flow chart

Among the 39 PLHIV, ten refused to participate (26%), four had contra-indications (denture, lead in the teeth) (10%), and four were unreachable (10%). Finally, 21 PLHIV were included, but one PLHIV had a massive congenital pathology discovered during the MRI scan and was finally excluded. Among the 50 HIV-negative subjects, eight refused to participate (16%), and four had contraindications (denture, lead in the teeth) (8%), and twelve were unreachable (24%).

Finally, a total of 20 PLHIV and 26 HIV-negative subjects were included.

Characteristics of the sample

Participant's characteristics are presented in Table 1. No statistical difference was observed between groups in age, gender, education level, and marital status; PLHIV were significantly more frequently unemployed than HIV-negative subjects (65% vs. 26.9%, $p = 0.02$).

Concerning medical issues, almost one-third of the participants (28.3%) had hypertension, and reported tobacco use, but no significant difference between the groups was observed. Other comorbidities were less prevalent (<15%) in the whole sample.

Concerning HIV medical data, the median (IQR) duration of HIV infection was 12.3 years (9.9–16.2). Ten percent (10.0%) were on stage C at ART initiation. Median CD4 was 571 (373–1029) cells/µl and median Nadir CD4 was 144 (61–201) cells/µl. Only two patients had a detectable viral load but under 350 copies/ml at the time of evaluation. Seventy percent (70%) received the standard first-line combination (3TC — lamivudine, TDF — tenofovir, EFV — efavirenz) for their current ART. Only 10% had AZT in their current ART, whereas 70% had AZT, DDI, or D4T in their initial ART.

Feasibility and acceptability

The median time between inclusion visit and MRI scan was short: eight days (IQR: 3–75 days; minimum: one day; maximum: 226 days). Specific access to the scanner has been granted by the Principal hospital management once a week, each Saturday morning. A quarter of the PLHIV subjects refused to participate in the study (25.6%), whereas only 15.4% of the HIV-negative subjects refused. Even if some participants reported that the MRI exam's duration was a little long, the participants' satisfaction was globally great.

We did not find significant differences between PLHIV included and not included in the MRI study (data not shown).

Global brain volumes and WMH volumes

No significant difference was observed between PLHIV and controls for global and WMH volumes (Table S1 in Supplementary data).

Atrophy prevalence and associated factors

The overall prevalence of atrophy (Koedams score ≥2) was 19.6% (CI95%: 8.1–31.0%), with a higher prevalence in PLHIV (30% (CI 95%: 9.9–50.1%)) compared to HIV-negative subjects (11.5% (CI 95%: 0.0–23.8%)) but the difference did not reach statistical significance (p = 0.15) (Table S2 in Supplementary data).

In univariate models (Table 2), being HIV+ (OR = 3.3, CI 95%: 0.7–15.3), being unemployed (OR = 3.3, CI 95%: 0.7–15.3), having hypertension (OR = 2.5, CI 95%: 0.6–11.3), and being a tobacco user (current or previous) (OR = 2.5, CI 95%: 0.6–11.3) tend to be associated with atrophy. Women tend to have a lower risk of atrophy than men (OR = 0.3, CI 95% = 0.1–1.3).

In the multivariate model, being unemployed (aOR = 24.1 CI 95%: 1.7–345.1) and having hypertension (aOR = 14.8, CI 95%:1.3–166.5) were significantly associated with atrophy (GoF, p = 0.88) whereas being a woman tended to be a protective factor (aOR = 0.02, CI 95%: (0.0–0.4).

Severe WMH prevalence and associated factors

The overall prevalence of severe WMH was 30.4% (CI 95%: 17.1–43.7%), without a significant difference between the groups (PLHIV: 25% (CI 95%: 6.0–43.9%) vs HIV-negative subjects: 34.6% (CI 95%: 16.3–52.9%), p = 0.54) (Table S1 in Supplementary data).

In univariate models, age ≥60 years was the only factor significantly associated with severe WMH (OR = 5.5 (CI 95%: 1.4–21.9), p = 0.02) (Table 3). Being a woman (OR = 3.7, CI 95%: 0.9–15.7), having hypertension (OR = 2.7 CI 95%: 0.7–10.3), and having hyperlipidemia (OR = 3.9 CI 95%: 0.7–20.4) tend to be associated with severe WMH. Tobacco users (current or previous) tended to have less WMH than others (OR = 0.1 (0.0–1.1), p = 0.06).

In the multivariate analysis, age remains the only factor associated with WMH.

Associations between atrophy or severe WMH and HIV outcomes

No significant association was observed between atrophy or severe WMH and HIV outcomes (Table S3 in Supplementary data), except a trend for an association between atrophy and being at CDC stage C (p = 0.08) and having AZT molecules in current ART (p = 0.08).

Discussion

Our results highlight the feasibility and the acceptability of high-resolution MRI scans acquisition in Senegal. As the first result, we observed a high prevalence of abnormalities

but no significant difference between patients well controlled for HIV infection (CD4 > 500/mm, HIV RNA < 50 copies/mL) and HIV-negative subjects. Unemployment and hypertension were the main factors associated with brain atrophy in this study, whereas the female gender seemed to be protective. Only age was associated with severe WMH.

Concerning feasibility and acceptability, our results are encouraging, with acquisitions of high resolution scans on a 1.5T machine, the reasonable time between inclusion and MRI exams, and a specific MRI vacation at the participating hospital service. However, as this type of examination is relatively uncommon in Senegal, the refusal rate was moderate (25% in PLHIV), suggesting the need to demystify brain MRI scans to limit patients' anxiety. Future studies should take this into account when calculating their sample size.

The prevalence of atrophy was high in the sample, with associated factors usually observed in the literature in Western countries' general population. Among cardiovascular risk factors, hypertension is a risk factor for vascular dementia and has been shown to be associated with cerebral atrophy in aging (Firbank et al., 2007; Wiseman et al., 2004). HIV tended to be associated with atrophy in univariate analyses, but this finding must be assessed in a larger sample. In previous studies using quantitative methods, cortical atrophy was observed, even in virologically suppressed PLHIV with a similar age range as ours (Becker et al., 2011; Clifford et al., 2017; Janssen et al., 2015). However, in those studies, participants reported alcohol and/or drug use and comorbidities that clearly could have impacted brain integrity. One study in South Africa also reported significantly lower volumes in PLHIV than in HIV-negative subjects (Heaps et al., 2012). In this publication, the participants were younger, with a significant demographic difference between both groups (particularly in age) and also with patients presenting different HIV-related characteristics (inclusion of clade C HIV, ART naïve and CD4 < 500 cells/μ) compared to ours. The absence of age effects could be due to the small sample size and the limited number of PLHIV aged above 65. Among HIV-related factors, we found an association between atrophy and AZT in current ART. As old nucleoside reverse transcriptase inhibitors are known to have significant toxicity and are still used in this population, certain precautions should be taken. However, due to the small sample size, we could not interpret those results, however they could inform future studies.

The prevalence of WMH was high in our sample, with a main effect of age and no significant impact of HIV status. The association between age and WMH has been described in the general population (Ovbiagele and Saver, 2006) and in PLHIV (McMurtray et al., 2008; Robinson-Papp et al., 2018; Seider et al., 2016). Concerning the impact of HIV status on WHM burden, no consensus could be reached from published data, mainly due to samples' characteristics. Publications from the United Kingdom and the Netherlands reported a higher burden of WMH in PLHIV than in HIV-negative subjects (Cole et al., 2018; Su et al., 2016) with no higher rates of changes after two years of follow-up (Cole et al., 2018). These samples included males in the large majority (>90%) and drug users. One study from France reported a higher prevalence of WMH in PLHIV than in HIV-negative subjects but did not clearly report the level of significance of this difference (Moulignier et al., 2018). More recent studies in western countries, with larger samples sizes, reported no significant WMH burden difference between PLHIV and HIV-negative subjects (Haddow et al., 2019; Sanford et al., 2019; Watson et al., 2017), and no rapid worsening of WMH burden

after two years of follow-up (Sanford et al., 2019). Those studies included demographically matched HIV-negative subjects and PLHIV with similar HIV medical characteristics (i.e., being on ART, virally suppressed, with high CD4 level and long disease duration), but different vascular risk factors than ours (i.e., less or high hypertension or tobacco use prevalence). Additional longitudinal studies are needed to evaluate the dynamic of these lesions in this population and confirm the impact of HIV status.

To our knowledge, this study represents the first opportunity to describe cerebral alterations in adults aged above 50 years old and living in West Africa, according to HIV status. A significant strength is the comparison of PLHIV brain structure to that of HIV-negative subjects with similar socio-demographic and medical comorbidities. Even in western countries, few studies include a control group. However, some limitations have to be mentioned. First, the principal limitation was the small sample size. As PLHIV and HIV-negative subjects had similar socio-demographic and comorbidities characteristics, we decided to group them in the statistical analyses to increase statistical power. Even though results could not be generalized, our findings can inform future studies to estimate power calculations for large-scale MRI studies evaluating cerebral alterations among PLHIV. Second, due to sample size limitations, quantitative explorations were limited. Third, the investigation of white matter integrity was limited as we did not perform diffusion tensor imaging. This type of sequence was unavailable on our MRI machine but might be included in future research.

Conclusion

Despite a limited sample size, our results report a high prevalence of atrophy and WMH in older west Africans, without a significant effect on HIV status. Moreover, as the prevalence of hypertension is high in PLHIV and HIV-negative subjects, further studies are needed to describe cardiovascular disease's impact on the brain in this population. Finally, as neuroimaging studies have contributed, and still do, to understand the pathophysiology of diseases, those studies could shed light on possible cerebral dysfunctioning mechanisms that sustain cognitive impairment in this population of West Africa as it gets older. For all these reasons, it is important to support MRI studies in West Africa, both in the general population and HIV patients. Identifying specific alterations will confirm the dominant pathological process to set up interventional studies of a bigger scale and give recommendations to better manage cognitive disorders in this population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of the sample.

	HIV-negative subjects		PLHIV		p*	Total	
	N	%	N	%		N	%
Total	26	100.0	20	100.0		46	100
Socio-demographic data							
Age					0.77		
50–59	14	53.8	12	60.0		26	56.5
60 and +	12	46.1	8	40.0		20	43.5
Gender					0.77		
Male	10	38.5	9	45.0		19	41.3
Female	16	61.5	11	55.0		27	58.7
Education level					0.15		
Secondary or more	15	57.7	7	35.0		22	47.8
Primary or less	11	42.3	13	65.0		24	52.2
Matrimonial situation					0.37		
In couple	18	69.2	11	55.0		29	63.1
Alone	8	30.8	9	45.0		17	36.9
Professional activity					0.02		
Employed	19	73.1	7	35.0		26	56.5
Not employed	7	26.9	13	65.0		20	43.5
Anthropometric and medical data							
Hypertension	8	30.8	5	25.0	0.75	13	28.3
Hyperlipidemia	5	19.2	2	10.0	0.45	7	15.2
Diabetes	1	3.8	1	5.0	1.00	2	4.3
Hepatitis B or C	0	0.0	3	15.0	0.08	3	6.5
Tuberculosis	0	0.0	3	15.0	0.08	3	6.5
History of trauma	1	3.8	0	0.0	1.00	1	2.2
History of neurological diseases	0	0.0	1	5.0	0.44	1	2.2
Hazardous alcohol drinkers	1	3.8	0	0.0	1.00	1	2.2
Tobacco use (current/former)	7	26.9	6	30.0	1.00	13	28.3

	HIV-negative subjects		PLHIV		p*	Total	
	N	%	N	%		N	%
Severe depressive symptoms	1	3.8	1	5.0	1.00	2	4.3

Abbreviations. PLHIV: people living with HIV.

*Fisher's Exact Test two-sided Pr <=P.

Table 2

Factors associated with atrophy in the whole sample.

		Univariate models		Multivariate model		V de Cramer
	Atrophy cases n/N (%)	**OR (CI 95%)**	**p**	**aOR (CI 95%)**	**p**	
HIV status			0.13			
HIV−	3/26 (11.5)	1				
HIV+	6/20 (30.0)	3.3 (0.7–15.3)				
Age			0.95		0.30	0.01
50–59	5/26 (19.2)	1		1		
60 and +	4/20 (20.0)	1.1 (0.2–4.6)		3.8 (0.3–47.1)		
Gender			0.09		**0.01**	−0.25
Male	6/19 (31.6)	1		1		
Female	3/27 (11.1)	0.3 (0.1–1.3)		0.02 (0.0–0.4)		
Education level			0.34		0.07	−0.14
Primary or less	6/24 (25.0)	1		1		
Secondary or more	3/22 (13.6)	0.5 (0.1–2.2)		0.1 (0.01–1.2)		
Professional activity			0.13		**0.02**	0.23
Employed	3/26 (11.5)	1		1		
Unemployed	6/20 (30.0)	3.3 (0.7–15.3)		24.1 (1.7–345.1)		
Hypertension					**0.03**	0.18
No	5/33 (15.1)	1	0.24	1		
Yes	4/13 (30.8)	2.5 (0.6–11.3)		14.8 (1.3–166.5)		
Hyperlipidemia			0.70			
No	8/39 (20.5)	1				
Yes	1/7 (14.3)	0.6 (0.1–6.2)				
Tobacco use (current/former)			0.24			
No	5/33 (15.1)	1				
Yes	4/13 (30.8)	2.5 (0.6–11.3)				

Abbreviations: aOR: Adjusted Odd Ratio, CI: confidence interval, OR: Odd Ratio.

Table 3

Factors associated with severe white matter hyperintensities (WMH) in the whole sample.

		Univariate models		Multivariate model		
	WMH cases n/N (%)	**OR (CI 95%)**	**p**	**OR (CI 95%)**	**p**	
HIV status			0.48			
HIV−	9/26 (34.6)	1				
HIV+	5/20 (25.0)	0.6 (0.2–2.3)				
Age			**0.02**		**0.02**	0.37
50–59	4/26 (15.4)	1		1		
60 and +	10/20 (50.0)	5.5 (1.4–21.9)		5.5 (1.4–21.9)		
Gender			0.08			
Male	3/19 (15.8)	1				
Female	11/27 (40.7)	3.7 (0.9–15.7)				
Education level			0.40			
Primary or less	6/24 (25.0)	1				
Secondary or more	8/22 (36.4)	1.7 (0.5–6.1)				
Hypertension			0.15			
No	8/33 (24.2)					
Yes	6/13 (46.1)	2.7 (0.7–10.3)				
Hyperlipidemia			0.11			
No	10/39 (25.6)					
Yes	4/7 (57.1)	3.9 (0.7–20.4)				
Tobacco use (current/former)			0.06			
No	13/33 (39.4)					
Yes	1/13 (7.7)	0.1 (0.0–1.1)				

Abbreviations: aOR: Adjusted Odd Ratio, CI: confidence interval, OR: Odds Ratio, WMH: White Matter Hyperintensities.