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Cumulative HIV Viremia Copy-Years and Hypertension in People Living with HIV

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Abstract

Background: Evidence regarding the association between HIV viral load (VL) and hypertension is inconsistent. In this study, we investigated the relationship using viremia copy-years (VCY), a cumulative measure of HIV plasma viral burden.

Methods: Data were analyzed for 686 PLWH in the Florida Cohort Study, who had at least five years of VL data before the baseline. VL data were extracted from Enhanced HIV/AIDS Reporting System (eHARS) and used to define peak VL (pVL), recent VL (rVL), and undetectable VL (uVL: rVL<50copies/mL). A five-year VCY ($\log_{10}$ copy × years/mL) before the baseline investigation, was calculated and divided into 5 groups (<2.7, 2.7–3.7. 3.8–4.7, 4.8–5.7 and >5.7) for analysis. Hypertension was determined based on hypertension diagnosis from medical records. Multivariable logistic regression was used for association analysis.

Results: Of the total sample, 277 (40.4%) participants were hypertensive. Compared to the participants with lowest VCY (<2.7 $\log_{10}$ copy × years/mL), the odds ratios (OR) and 95% confidence interval [95% CI] for hypertension of the remaining four groups, in order, were 1.91 [1.11, 3.29], 1.91 [1.03, 3.53], 2.27 [1.29, 3.99], and 1.25 [0.65, 2.42], respectively, controlling for confounders. The association was independent of pVL, rVL, and uVL, each of which was not statistically significant associations with hypertension.

Conclusion: Persistent HIV infection is a risk factor for hypertension among PLWH. Information provided by VCY is more effective than single time-point VL measures in

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STANDARD OF REPORTING

The study conforms to the STROBE guidelines.

AVAILABILITY OF DATA AND MATERIALS

The authors confirm that the data supporting the results and findings of this study are available within the article.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

investigating HIV infection-hypertension relationship. The findings of this study support the significance of continuous viral suppression in hypertension prevention among PLWH.

Keywords

Cumulative viremia; copy-years; hypertension; HIV; viral load; virological suppression

1. INTRODUCTION

Chronic health conditions have emerged as a new health challenge for persons living with HIV (PLWH), along with the success of antiretroviral therapy (ART) and increases in survival after HIV diagnosis [1–5]. As a common risk factor for cardiovascular diseases (CVDs), hypertension is prevalent among PLWH [5–15] and increases with an incidence ranging from 26–220 per 1000 person-years [7, 16–23]. Plasma HIV viral load (VL) or HIV RNA is used as an integral clinical indicator in patient care and an independent predictor of HIV infection-related morbidity and mortality in research [24–28]. The effect of plasma HIV RNA has largely been ascribed to the sustained de novo viral replication, which is responsible for the irreversible damage to the immune system, inflammatory responses, and immune system activation [29–31].

The risk of hypertension among people with HIV is attributable to a combination of the traditional risk factors, HIV-specific factors, and side effects of ART agents [11, 14, 20, 32–36]. HIV infection has been related to some potential mechanisms of hypertension, such as immune activation and chronic low-grade inflammation [37–41]. The pro-inflammatory effects of HIV infection on vascular endothelium activate reactive oxygen species that further induce endothelial damage, vasoconstriction, reduced endothelium-dependent relaxation, and vascular stiffness [37, 38, 42–44]. Other pathophysiologic mechanisms for hypertension include microbial translocation, immune suppression/ reconstitution, viral tropism, lipodystrophy, adipokines, and HIV-related renal disease [20, 44–47]. Some studies suggest that successful HIV virological suppression was associated with the improvement of immune function, reduction of systemic inflammatory markers, and reduction in CVD events [48]. However, a careful examination of the findings revealed that the epidemiological evidence supporting the association between HIV VL and hypertension is either limited or inconsistent [37, 49, 50]. More research is needed to advance our understanding of the relationship between HIV infection and the risk of hypertension to develop evidence-based and effective intervention strategies for hypertension prevention among PLWH.

One issue common among the published studies is that HIV infection in these studies was often measured with viral load data collected at one point in time, such as peak VL (pVL), recent VL (rVL), undetectable viral load (uVL) and viral suppression [37, 49–51]. Relative to single time-point measures, a cumulative measure of VL may be more effective to reflect the process of systemic inflammation and immune activation after HIV infection [29]. Therefore, a cumulative measure may be more relevant than a single time-point measure to examine the relationship between HIV infection and hypertension.

Repeated VL measures from diverse sources make it possible for researchers to derive cumulative measures of long-term exposure to viral replication. One typical measure is the viremia copy-years (VCY). As the term indicates, VCY measures HIV infection by summing up VL measured at multiple time points over time. It provides a proxy of cumulative HIV viremia, and is a strong predictor of all-cause mortality among PLWH [52–55]. In theory, VCY may also be associated with hypertension [29], yet no reported studies have used this measure in hypertension research among PLWH. We conducted this study with an attempt to fill the data gap.

2. METHODS

2.1. Study Setting and Participants

This is a secondary analysis of data extracted from the Florida Cohort Study (http://sharc-research.org/). The Florida Cohort Study is an NIH-funded project to identify influential factors to improve HIV care outcomes with a diverse sample of PLWH. Participants were enrolled between 2014–2017 from multiple HIV clinics and community settings across the State of Florida, including Lake City, Gainesville, Tampa, Orlando, Sanford, Ft. Lauderdale, and Miami. Detailed information of this cohort has been previously described [56, 57].

With the assistance of the Florida Department of Health, survey data collected by the Florida Cohort Study were linked with laboratory data on VL and CD4+ T cell counts in the Enhanced HIV/AIDS Reporting System (eHARS) and data on hypertension diagnosis, antiretroviral medications, antihypertensive medication, and height and weight in the medical record.

We included participants who had been diagnosed with HIV for at least 5 years prior to the baseline investigation, who had at least 2 HIV viral load test results during the 5 years, and who had data to ascertain hypertension diagnosis. Hypertension was defined using the International Classification of Diseases, 9th Revision (ICD-9: 401.xx). In order to avoid secondary hypertension and hypertension-related comorbidities confounding the potential association between hypertension and VCY, we excluded patients with secondary hypertension and relevant comorbidities, including hypertensive heart disease (402.xx), hypertensive renal disease (403.xx) hypertensive heart and renal disease (404.xx) and secondary hypertension (405.xx). Finally, a total of 686 participants were included in this study.

Written informed consent was obtained from individual participants of the Florida Cohort study. Approval of this study was obtained from the Institutional Review Boards (IRB) at the University of Florida, Florida International University, and the Florida Department of Health.

2.2. Definition and Calculation of VCY

VCY was the primary predictor variable and it was calculated based on the VL measures over 5 years prior to the baseline. The calculation was completed following the standard method by summing up the areas under the VL time series using the trapezoidal rule (Fig. 1) [55, 58, 59]. Since the number of visits J, the timing of visits t(j) and VL value at time j

VL(j) vary by participant, VCY was estimated using the following formula and expressed in copies × years per milliliter (cells × years/ml):

$$\mathrm{VCY(J)} = \sum_{j=1}^{J} \frac{[VL(j-1) + VL(j)] \times [t(j) - t(j-1)]}{2} \quad (1)$$

The calculated VCY provided a monotonic increasing measure of cumulative plasma HIV viremia over time. Thus, VCY for a participant can thus be described as the sum of areas for each trapezoid consisting of 2 consecutive VL values and the time interval between the 2 VL measures (Fig. 1). A person with a VCY of 10,000 copy-years is equivalent to being exposed to 10,000 copies per milliliter of VL each day for 1 year or 1000 copies per milliliter VL each day for 10 years of HIV-RNA.

We selected 5 years because findings of a previously reported study showed that VCY calculated using time intervals of 3–8 years better-predicted mortality risk than complete VL history and single time-point VL measures [53].

2.3. Other HIV Infection Measures

Three more HIV infection measures were used. The peak viral load (pVL) was defined as the maximum value of VL since confirmed HIV diagnosis. The recent viral load (rVL) was defined as the VL measurement closest to the baseline investigation. Undetectable viral load (uVL) was defined as rVL< 50 copies/mL. These three measures were used as secondary predictors to be compared with VCY in predicting hypertension.

2.4. Other Variables

The CD4+ T-cell count closest to the baseline investigation was extracted from eHARS for analysis. The duration of HIV diagnosis was a difference of years between HIV diagnosis and baseline investigation. Depression was defined based upon the depression diagnosis from medical records. Other covariates were collected through questionnaires (age, gender, race/ethnicity, current smoking, and drinking) or extracted from their medical records (diabetes, status of antiretroviral therapy, and the use of antihypertensive medications). Heavy drinkers was defined as >14 drinks/week for male, and >7 drinks/week for female.

2.5. Statistical Analysis

Participants with and without hypertension were compared first using Student t-test for continuous variables and chi-square test for categorical variables. Correlations between VCY, pVL, rVL, and uVL were assessed using Spearman's rank correlation. Separate multivariable logistic regression models for different VL measures were constructed to examine their associations with hypertension. In addition to continuous VCY, the categorized VCY in five groups was analyzed with four cutoffs: 2.7 $\log_{10}$ (500 copy-years), 3.7 $\log_{10}$ (5,000 copy-years), 4.7 $\log_{10}$ (50,000 copy-years), and 5.7 $\log_{10}$ (500,000 copy-years). Likewise, pVL was categorized into five groups with cutoffs of 2.3 $\log_{10}$ (200 copies/mL), 3.3 $\log_{10}$ (2,000 copies/mL), 4.3 $\log_{10}$ (20,000 copies/mL), and 5.3 $\log_{10}$ (200,000 copies/mL), and rVL was categorized into four groups with cutoffs of 1.3 $\log_{10}$ (20 copies/mL), 2.3 $\log_{10}$ (200 copies/mL), and 3.3 $\log_{10}$ (2,000 copies/mL).

In the multivariate logistic regression analyses, the following covariates were controlled: age, sex, race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic-black, and other), and other variables significantly associated with hypertension in bivariate analysis, including BMI (kg/m^2), diabetes, CD4+ count (≥500 vs. <500 cells/mm^3), and years of HIV infection (>10 vs. ≤10 years).

To avoid the potential confounding effects of antihypertensive medications, a sensitivity analysis was performed with patients categorized into three groups: no-hypertension, hypertension treated, and hypertension untreated. We employed multinominal logistic regression to test the association with CVY for hypertension treated vs. no hypertension and hypertension untreated vs. no hypertension. In the last step of the analysis, a logistic regression model with all four VL measures (*i.e.* VCY, pVL, rVL, and uVL) being included was constructed to assess the independent association of VCY with -hypertension after considering the effect of other three single time-point VL measures.

3. RESULTS

3.1. Participant Characteristics

Participant characteristics are summarized in Table 1. A total of 686 participants were included in this study. Among 277 hypertensive participants, 178 (64.3%) used antihypertensive medications. The mean age was 46.8 (SD=11.2) years and more than half were males. The median VCY was 4.4 log_{10} copy × year/mL [Interquartile range (IQR): 3.0, 5.4 log_{10} copy × year/mL]. The medians of pVL and the rVL were 3.0 log_{10} copies/mL [IQR: 2.0, 3.0 log_{10} copies/mL] and 1.3 log_{10} copies/mL [IQR: 1.3, 2.2 log_{10} copies/mL] respectively. Of all participants, 450 (65.6%) had viral load undetectable. Compared with normotensive participants, those with hypertension were older and more likely to be black and female ($p<0.05$). Hypertensive participants had higher BMI, CD4+ T cell counts, and VCY, and longer years living with a diagnosis of HIV than normotensives ($p<0.01$).

3.2. Correlations of VCY, rVL, pVL, and uVL

The log10 transformed VCY had a bimodal distribution with two peaks at 2.5–3.0 and 4.8–6.0, respectively. The distribution of pVL (log10 transformed) was relatively stable except for an increase between 4.5 – 5.5. The distribution of rVL (log10 transformed) was asymmetric and skewed distributed with the majority falling at 1.3 or less (Fig. 2). The rank correlation matrix for the various measures of VL is provided in Table 2. In summary, these measures of VL were positively correlated with each other with different extent.

3.3. Association between VCY and Hypertension

The associations with hypertension from separate logistic regressions for VCY, pVL, rVL, and uVL are given in Fig. (3) and Table 3. Of these four viral-load measures, VCY was significantly associated with hypertension (Fig. 3a and Table 3). Compared with the participant with VCP<2.7 log10 copy × years/mL, the odds ratio (OR) and the [95% CI] for participants with VCP of 2.7 – 3.7, 3.8 – 4.7, 4.8 – 5.7, and >5.7 log10 copy × years/mL were 1.91 [1.11, 3.29], 1.91 [1.03, 3.53], 2.27 [95%CI=1.29, 3.99], and 1.25 [95%CI=0.65, 2.42], respectively, after adjusting for demographic (age, sex, race/ethnicity) and other key

factors (BMI, diabetes, CD4+ T cell count, and years of HIV diagnosis). Sensitivity analysis showed similar results for hypertensive patients with and without treatment in comparison to normotensive people (Appendix Table 1). When VCY was used as a continuous variable, the association with hypertension was not statistically significant (OR [95% CI] = 1.08 [0.94, 1.24]) (Fig. 3a).

No significant relationship was observed between the other three viral load measures and hypertension, including the peak viral load, the most recent viral load and whether the virus was detected or not (Fig. 3b–3d and Table 3).

All models were adjusted for age, sex, race (Hispanics, non-Hispanic whites, non-Hispanic-blacks, and others) BMI (kg/m^2), diabetes, CD4+ T cell count (≥500 vs. <500 cells/mm^3), and years of HIV diagnosis (>11 vs. ≤11years).

The model was adjusted for age, sex, race (Hispanics, non-Hispanic whites, non-Hispanic-blacks, and others) BMI (kg/m^2), diabetes, CD4+ T cell count (≥500 vs. <500 cells/mm^3), and years of HIV diagnosis (>11 vs. ≤11years).

4. DISCUSSION

To our knowledge, this is the first study that assessed the relationship between cumulative exposure to HIV viremia and hypertension among PLWH using VCY, a well-established and widely accepted measure in research. With this measure, a patient's cumulative HIV exposure was measured using VL data collected from routine HIV clinical blood draws for care. Although various VL measures are positively correlated with each other, their function to predict hypertension risk differed.

In our study, only VCY was significantly associated with hypertension, and this relationship was independent of pVL, rVL, and uVL. This association would not be detected if any of the three single time-point VL measures were used. Our findings support that VCY can provide more useful information beyond single time-point measures in investigating HIV infection-hypertension relationship. The findings of this study demonstrate the significance of continuous suppression of HIV VL in the prevention of hypertension for those living with a diagnosis of HIV.

A number of recent observations have examined the prognostic values of VCY measures. Some demonstrated improved prognostic performance of VCY over that of single time-point VL, and showed VCY as an independent predictor for AIDS mortality and morbidity [54, 60–62]. Some showed that the prognostic effect of VCY was dependent on single time-point VL measures and showing a stronger predictive effect of mortality of the single time-point VL measures than the accumulative VCY [59, 63]. We found two studies in which VCY was used to predict non-AIDS related clinic events. Results from these studies showed significant relationships between VCY and age-related declines in grip strength and acute myocardial infarction [60, 61]. Findings from our study add new data demonstrating the advantages of using VCY over other measures to examine the relationship between HIV infection and the risk of hypertension among PLWH.

Findings of our study suggest it is not the HIV exposure at a point in time but the cumulative exposure over time to elevate the risk of hypertension. The inconsistent findings regarding the relationship between HIV VL and hypertension [64–66] could be due to the use of one single time-point measure of VL while large variations in VL are possible for individual patients. Therefore, researchers must consider the relevance to the outcome variable when selecting a predictor [59, 67]. When examining an acute outcome, one-time measure of VL prior to the occurrence of the outcome, such as the most recent VL may be the most appropriate. However, hypertension is a chronic condition and it involves a long process from systematic inflammation, immune system activation, to arterial sclerosis, which occurs over a long period of time [59]. Therefore, VCY provides the most appropriate measure of exposure to HIV infection, compared to the other single time-point measures.

There is not yet a consensus on the routine use of VCY in HIV care practice, our findings serve as proof of the concept that such measures should be used to improve clinicians' ability to identify patients who are at increased risk of hypertension. It implies that maintaining a low level of VL may lower the risk of hypertension among PLWH. Studies have shown a persistently elevated risk of hypertension among PLWH than HIV-controls despite viral suppression [39, 68, 69]. These conclusions, however, are based upon single time-point VL measure with the validity questionable.

It is worth noting that VCY>5.7 log10 copy × years/mL, the highest CVY group was not significant because the 95% CI included zero. This is probably due to the fact that participants with higher viral loads are also be more likely in the early stage of HIV infection, while hypertension often occur years later after infection. When VCY was analyzed as a continuous variable, the relationship with hypertension was not statistically significant. This result is reasonable because the VCY measure is bimodal rather than normally distributed as shown in Fig. (2) and the relationship between VCY and hypertension is not linear, based on results from the categorized VCY presented above. Additional studies are needed with discrete and chaotic models capable of considering this characteristic of the data, such as the cusp catastrophe modeling method [70–74]. Further, we selected a 5-year time frame to calculate VCY according to the existing literature regarding all-cause mortality [53]. How long of a meaningful window of a PLWH's VL history should be included in VCY for optimal prognostic performance in predicting hypertension risk needs to be explored in more detail.

This study has limitations. Although we assessed cumulative HIV burden, the temporality of when the hypertension diagnosis occurred is unknown. Studies should be done using longitudinal data considering temporal sequences and time-dependent covariates. Studies in which VCY showed a better predictive of mortality were generally conducted among ART-initiating people, [54, 55, 63] whose hypertension risk is likely to be affected by the therapy [6, 7, 75, 76]. Because of data limitations, we were not able to separate the impact of cumulative HIV infection from ART initiation and ART regimens on the risk of hypertension. Data was unavailable to test the association of VCY with the severity of hypertension, such as elevated blood pressure, stage 1 hypertension, and stage 2 hypertension. In addition, although we have controlled established confounders available in our dataset, unmeasured confounders, such as physical activity, diet, and serum lipid

measures were not taken into account. Finally, caution should be taken when generalizing our findings to other studies since participants of the study are persons living with an HIV diagnosis in Florida.

CONCLUSION

By assessing cumulative exposure to HIV viremia, the results of our study suggest that long-term unsuppressed HIV may be an independent risk factor of hypertension among PLWH. Keeping HIV VL continuously suppressed not only contributes to improving AIDS-related mortality and morbidity but also can be used as an effective strategy for hypertension prevention. Future research is necessary to explore how the correlation with VCY would be impacted by the severity of hypertension. In addition, future studies are needed to discover the impact of viral clade and HIV mutations on the relationship of cumulative HIV exposure and hypertension.

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APPENDIX

Table 1.

Association of viremia copy-years (cells × years/ml) and hypertension by the use of antihypertensive medication.

Variables	OR	95% CI	
		Low	High
Hypertension treated vs. no hypertension			
~ 2.7 $\log_{10}$	1.00	-	-
~ 3.7 $\log_{10}$	2.06	1.22	4.39
~ 4.7 $\log_{10}$	2.11	1.12	4.63
~ 5.7 $\log_{10}$	2.91	1.68	6.64
> 5.7 $\log_{10}$	1.54	0.85	4.21
Hypertension untreated vs. no hypertension			
~ 2.7 $\log_{10}$	1.00	-	-
~ 3.7 $\log_{10}$	1.81	1.02	2.96
~ 4.7 $\log_{10}$	1.68	0.74	3.26
~ 5.7 $\log_{10}$	2.02	1.03	3.06
> 5.7 $\log_{10}$	0.77	0.80	3.77

CI: Confidence Interval; OR: Odds Ratio. Odds ratio was estimated using multinominal logistic regression, controlling for age, sex, race (Hispanics, non-Hispanic whites, non-Hispanic-blacks, and others) BMI (kg/m^2), diabetes, CD4+ T cell count (≥500 vs. <500 cells/mm^3), and years of HIV diagnosis (>11 vs. ≤11years).

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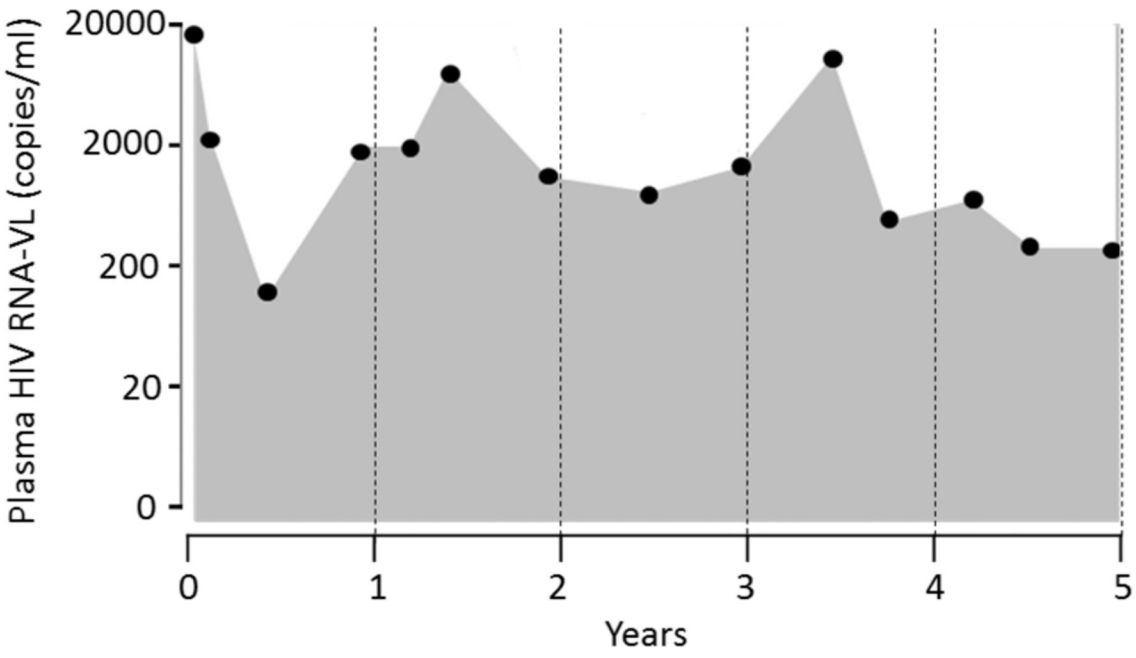

Fig. (1).
Example calculation of 5-year viremia copy-years.

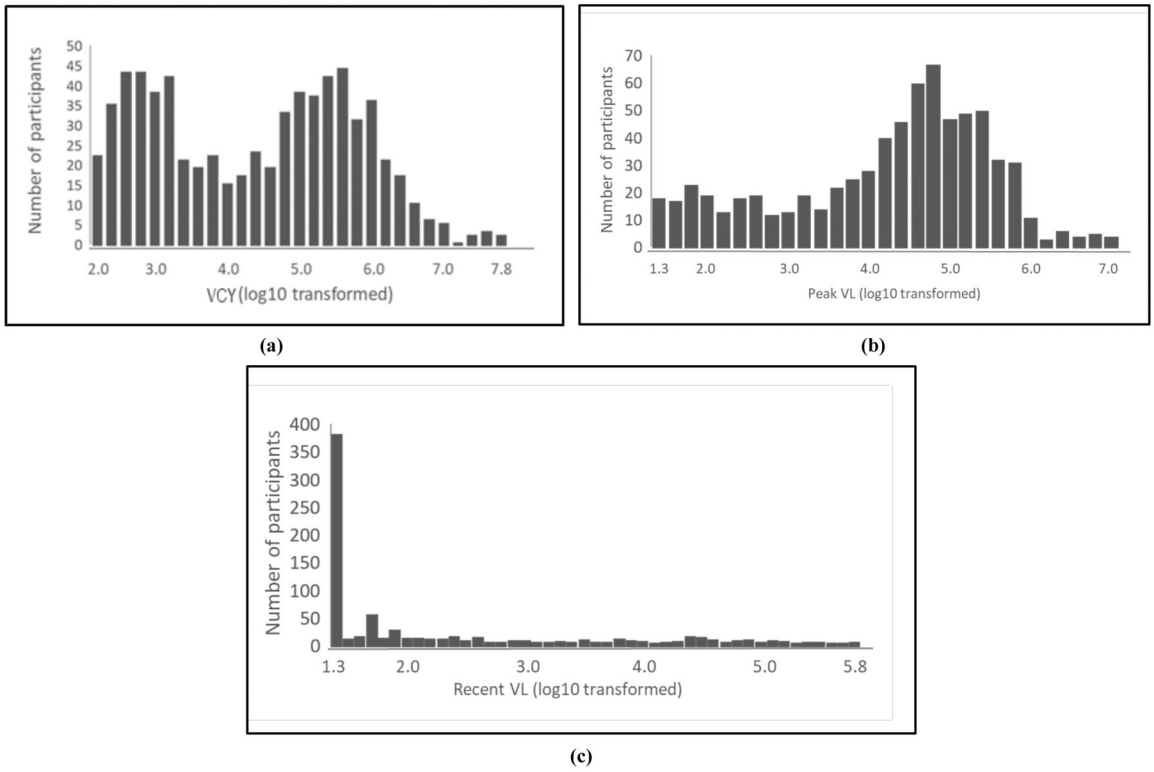

Fig. (2).
Distribution of viremia copy-years (**a**), peak viral load (**b**), the most recent viral load (**c**).

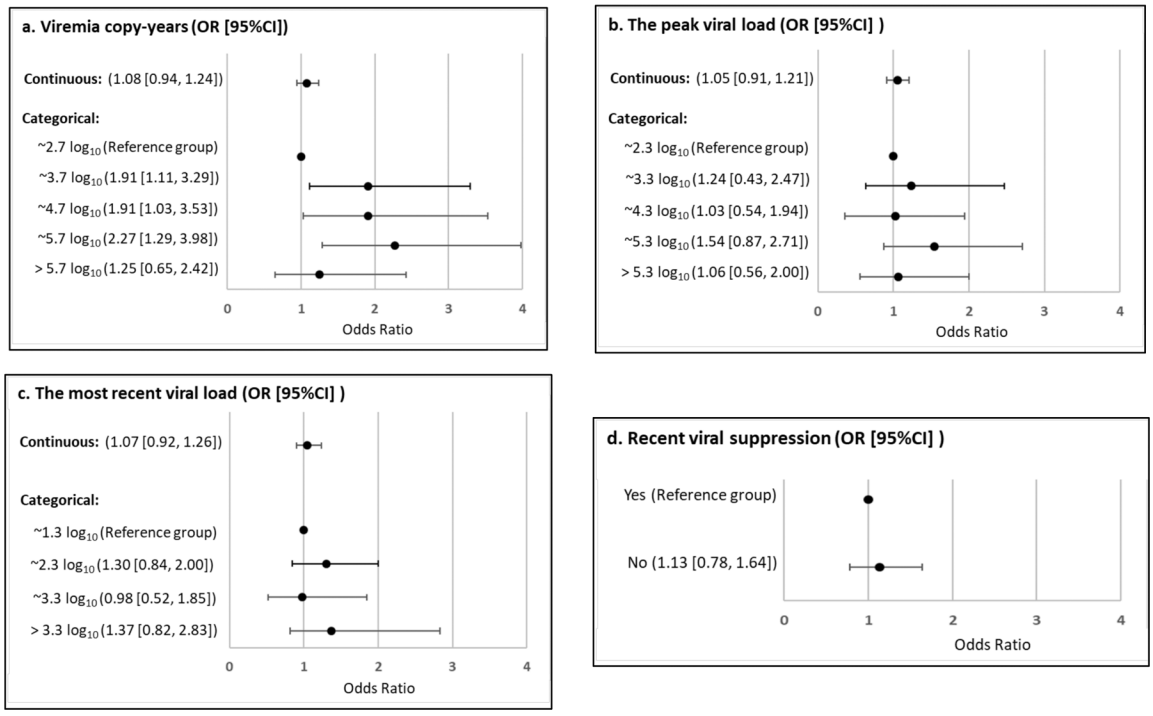

Fig. (3).

Results of separate multivariable logistic regression models for (**a**) viremia copy-years, (**b**) peak viral load, (**c**) the most recent viral load, and (**d**) undetectable viral load.

Table 1.

Participant characteristics

Variables	Participants (n=686)	Hypertensive (n=277)	Normotensive (n=409)	p-value
Sex, n (%)				<0.01
Male	442 (64.4)	162 (58.5)	280 (68.5)	
Female	244 (35.6)	115 (41.5)	129 (31.5)	
Race/ethnicity, n (%)				<0.01
Non-Hispanic whites	151 (22.0)	44 (15.9)	69 (16.6)	
Non-Hispanic blacks	395 (57.6)	44 (15.9)	107 (26.2)	
Hispanics	112 (16.3)	185 (66.8)	210 (51.3)	
Others	28 (4.1)	4 (1.4)	24 (6.9)	
Current smoking, n (%)				0.24
Yes	351 (51.2)	134 (48.4)	217 (53.1)	
No	335 (48.8)	143 (51.6)	192 (46.9)	
Heavy drinking, n (%)				0.34
Yes	63 (9.2)	29 (10.5)	34 (8.3)	
No	623 (90.8)	248 (89.5)	375 (91.7)	
Diabetes, n (%)				<0.01
Yes	88 (12.8)	63 (22.7)	25 (6.11)	
No	598 (87.2)	214 (77.3)	384 (93.9)	
Depression				0.54
Yes	99 (14.5)	42 (15.2)	59 (14.5)	
No	585 (85.5)	235 (84.8)	350 (85.6)	
CD4 (cells/mm^3), n (%)				0.02
≥500	355 (51.3)	158 (57.0)	197(48.2)	
<500	331 (48.7)	119 (43.0)	212 (51.8)	
Currently on ART, n (%)				0.74
Yes	593 (86.4)	238 (85.9)	355 (86.8)	
No	93 (13.6)	39 (14.1)	54 (13.2)	
Undetectable viral load, n (%)				0.48

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Variables	Participants (n=686)	Hypertensive (n=277)	Normotensive (n=409)	p-value
Yes	450 (65.6)	186 (67.2)	264(64.6)	
No	236 (34.4)	91 (32.8)	145 (35.4)	
Use of antihypertensive medications				
Yes	-	178 (64.3)	-	-
No	-	99 (35.)	-	-
Age, mean (SD)	No	50.5 (9.7)	44.4(11.4)	<0.01
BMI, mean (SD)	28.3 (7.1)	29.9 (7.3)	27.1 (6.6)	<0.01
Years of HIV infection, median (IQR)	10 (5,17)	13 (7, 18)	10 (4, 15)	<0.01
pVL (log_{10} copies/mL), median (IQR)	3.0 (2.0, 3.0)	3.0 (2.0, 3.0)	3.0 (1.0, 3.0)	0.36
rVL (log_{10} copies/mL), median (IQR)	1.3 (1.3, 2.2)	1.3 (1.3, 2.0)	1.3 (1.3, 2.3)	0.76
VCY (log_{10} copy × year/mL), median (IQR)	4.4 (3.0, 5.4)	4.7 (3.0,6.3))	4.2 (2.9, 5.3)	<0.01

Note: ART: antiretroviral therapy; BMI: Body Mass Index; IQR Interquartile Range; SD: Standard Deviation; pVL: Peak Viral Load; rVL: the most Recent Viral Load; uVL: undetectable viral load; VCY: Viremia Copy-years.

Table 2.

Spearman's rank correlation matrix for variables measures of viral load.

Variable	VCY	pVL	rVL	uVL
VCY	1.00			
pVL	0.74*	1.00		
rVL	0.36*	0.31*	1.00	
uVL	0.31*	0.28*	0.79*	1.00*

Note:

*: p<0.01; pVL: Peak Viral Load; rVL: the most Recent Viral Load; uVL: undetectable viral load; VCY: Viremia Copy-years;

Table 3.

Results of one multivariable logistic regression model including viremia copy-years, peak viral load, the most recent viral load, and undetectable viral load.

Variables	Adjusted OR	95% CI	
		Low	High
Viremia copy-years			
~ 2.7 $\log_{10}$ (n=120)	1.00	-	-
~ 3.7 $\log_{10}$ (n=151)	1.93	1.09	3.44
~ 4.7 $\log_{10}$ (n=98)	2.06	1.01	4.23
~ 5.7 $\log_{10}$ (n=204)	2.14	1.05	4.36
> 5.7 $\log_{10}$ (n=113)	1.18	0.50	2.80
Peak VL			
~2.3 (n=85)	1.00	-	-
~3.3 (n=76)	1.00	0.49	2.07
~4.3 (n=124)	0.73	0.35	1.53
~5.3 (n=264)	1.04	0.51	2.11
>5.3 (n=137)	0.93	0.41	2.11
Recent VL			
~1.3 (n=369)	1.00	-	-
~2.3 (n=153)	1.29	0.74	2.25
~3.3 (n=55)	0.92	0.34	2.47
>3.3 (n=109)	1.34	0.54	3.35
Undetectable viral load			
Yes	1.00	-	-
No	0.94	0.45	1.96

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