Consequences of Low-Level Viremia by Sex Among People With HIV in the United States

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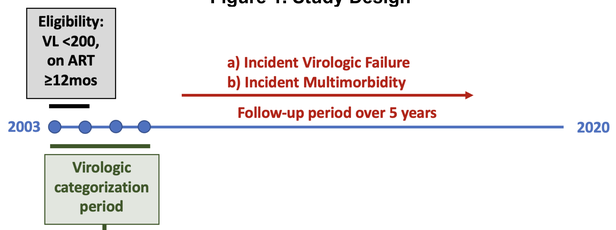
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BACKGROUND

- Low-level viremia (LLV) is common in people with HIV (PWH) on antiretroviral therapy (ART)
- LLV has been associated with adverse outcomes such as virologic failure, drug resistance mutations, and increased inflammation; however, impact of LLV on aging comorbidities is largely unknown
- Viremia copy-years (cumulative HIV viral load) has been associated with non-AIDS comorbidities, and are more pronounced in women than men
- We investigated the effect of intermittent LLV (iLLV) and persistent LLV (pLLV) on time to incident virologic failure and incident multimorbidity by sex

METHODS

Figure 1. Study Design



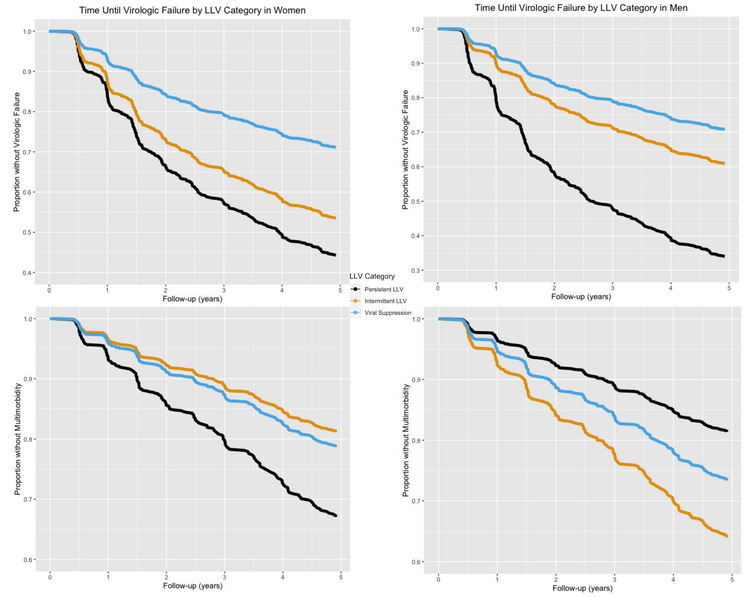
LLV Category	HIV-1 RNA (copies/mL)	Number of Visits
Virologic Suppression (VS)	Below lower limit of detection	All visits
Intermittent LLV (iLLV)	Detectable-199	Non-consecutive visits
Persistent LLV (pLLV)	Detectable-199	≥2 consecutive visits
Virologic Failure (VF)	≥200	Any visit

- Included PWH enrolled in the Multicenter AIDS Cohort Study (MACS) and the Women's Interagency HIV Study (WIHS) with study visits from 2003-2020
- Multimorbidity defined as ≥2 of 5 non-AIDS comorbidities (hypertension, dyslipidemia, diabetes, cardiovascular disease, chronic kidney disease)
- Adjusted Cox proportional hazards models used to evaluate time to incident virologic failure and incident multimorbidity
  - Included sex*LLV interaction term to evaluate the impact of sex on outcomes

Among all PWH, intermittent and persistent LLV were associated with incident virologic failure

Among women but not men, there was a trend toward increased risk of multimorbidity for those with persistent LLV

Figure 2. Survival Curves of Incident Virologic Failure and Multimorbidity Using Baseline Virologic Category, Stratified by Sex



CONCLUSIONS

- In a diverse cohort of US PWH, LLV was associated with an increased risk of developing VF, regardless of sex
- There was a trend toward pLLV being associated with an increased risk of multimorbidity in women but not in men
- Further research is needed to understand underlying mechanisms and to mitigate the adverse consequences of LLV in men and women

RESULTS

Table 1. Selected Baseline Demographic and Clinical Characteristics of Eligible People with HIV Overall and by Baseline Virologic Category

Selected Baseline Characteristics, Median (IQR) or n (%)	Total PWH n=2395	Virologic Suppression n=1469	Intermittent Low-level Viremia n=426	Persistent Low-level Viremia n=136	Virologic Failure n=364
Age, years	48 (41, 54)	48 (41, 54)	48 (42, 54)	50 (46, 56)	48 (41, 53)
Sex					
Female	1598 (67)	933 (64)	295 (69)	95 (70)	275 (76)
Male	797 (33)	536 (36)	131 (31)	41 (30)	89 (24)
Race/Ethnicity					
Black, non-Hispanic	1272 (53)	722 (49)	247 (58)	85 (63)	218 (60)
Hispanic	476 (20)	286 (19)	85 (20)	24 (18)	81 (22)
White, non-Hispanic	589 (25)	428 (29)	84 (20)	824 (18)	53 (15)
BMI ≥30 kg/m²	883 (37)	526 (36)	170 (41)	53 (38)	134 (37)
CD4, cells/μL	616 (454, 814)	636 (480, 836)	671 (486, 860)	662 (454, 819)	481 (282, 647)
ART Anchor Drug¥					
INSTI	645 (27)	393 (27)	120 (28)	45 (33)	87 (24)
PI	877 (37)	464 (32)	171 (40)	60 (44)	182 (50)
NNRTI	804 (34)	570 (39)	121 (28)	28 (21)	85 (23)

¥Categorized hierarchically INSTI>PI>NNRTI, such that a regimen containing an INSTI and PI would be categorized in the INSTI group, for example

Table 2. Hazard Ratios of Time to Incident Virologic Failure and Multimorbidity by Baseline Virologic Category Using Cox Proportional Hazards Models, Overall and Stratified by Sex

	Incident Virologic Failure Adjusted Hazard Ratio (95% Confidence Interval)*			Incident Multimorbidity Adjusted Hazard Ratio (95% Confidence Interval)**		
Virologic Category	**All n=1968**	**Women n=1304**	**Men n=664**	**All n=1123**	**Women n=773**	**Men n=350**
Virologic Suppression	REF	REF	REF	REF	REF	REF
Intermittent LLV	1.6 (1.2, 2.1)	1.8 (1.4, 2.4)	1.4 (0.9, 2.3)	1.1 (0.8, 1.6)	0.9 (0.6, 1.3)	1.4 (0.9, 2.4)
Persistent LLV	2.7 (1.9, 3.9)	2.4 (1.6, 3.6)	3.1 (1.7, 5.6)	1.1 (0.6, 1.9)	1.7 (1.0, 2.9)	0.7 (0.2, 1.9)

*Adjusted for age, ±sex (overall), ±LLV*sex (overall), race, socioeconomic status (SES), CD4, adherence, antiretroviral anchor
**Adjusted for age, ±sex (overall), ±LLV*sex (overall), race, SES, obesity, smoking, CD4, adherence, integrase inhibitor use

(LLV*sex p=0.4) (LLV*sex p=0.1)

We would like to acknowledge the MWCCS research participants and staff

Data in this manuscript were collected by the Multicenter AIDS Cohort Study (MACS) and the Women's Interagency HIV Study (WIHS), now the MACS/WIHS Combined Cohort Study (MWCCS).The contents of this publication are solely the responsibility of the authors and do not represent the official views of the National Institutes of Health (NIH). MWCCS (Principal Investigators): Atlanta CRS (Ighovwerha Ofotokun, Anandi Sheth, and Gina Wingood), U01-HL146241; Baltimore CRS (Todd Brown and Joseph Margolick), U01-HL146201; Bronx CRS (Kathryn Anastos, David Hanna, and Anjali Sharma), U01-HL146204; Brooklyn CRS (Deborah Gustafson and Tracey Wilson), U01-HL146202; Data Analysis and Coordination Center (Gypsyamber D'Souza, Stephen Gange and Elizabeth Topper), U01-HL146193; Chicago-Cook County CRS (Mardge Cohen and Audrey French), U01-HL146245; Chicago-Northwestern CRS (Steven Wolinsky, Frank Palella, and Valentina Stosor), U01-HL146240; Northern California CRS (Bradley Aouizerat, Jennifer Price, and Phyllis Tien), U01-HL146242; Los Angeles CRS (Roger Detels and Matthew Mimiaga), U01-HL146333; Metropolitan Washington CRS (Seble Kassaye and Daniel Merenstein), U01-HL146205; Miami CRS (Maria Alcaide, Margaret Fischl, and Deborah Jones), U01-HL146203; Pittsburgh CRS (Jeremy Martinson and Charles Rinaldo), U01-HL146208; UAB-MS CRS (Mirjam-Colette Kempf, Jodie Dionne-Odom, James B. Brock, and Deborah Konkle-Parker), U01-HL146192; UNC CRS (M. Bradley Drummond and Michelle Floris-Moore), U01-HL146194. The MWCCS is funded primarily by the National Heart, Lung, and Blood Institute (NHLBI), with additional co-funding from the Eunice Kennedy Shriver National Institute Of Child Health & Human Development (NICHD), National Institute On Aging (NIA), National Institute Of Dental & Craniofacial Research (NIDCR), National Institute Of Allergy And Infectious Diseases (NIAID), National Institute Of Mental Health (NIMH), National Institute On Drug Abuse (NIDA), National Institute Of Nursing Research (NINR), National Cancer Institute (NCI), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Deafness and Other Communication Disorders (NIDCD), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute on Minority Health and Health Disparities (NIMHD), and in coordination and alignment with the research priorities of the National Institutes of Health, Office of AIDS Research (OAR). MWCCS data collection is also supported by UL1-TR000004 (UCSF CTSA), UL1-TR003098 (JHU ICTR), UL1-TR001881 (UCLA CTSI), P30-AI-050409 (Atlanta CFAR), P30-AI-073961 (Miami CFAR), P30-AI-050410 (UNC CFAR), P30-AI-027767 (UAB CFAR), P30-MH-116867 (Miami CHARM), UL1-TR001409 (DC CTSA), KL2-TR001431 (DC CTSA). The authors gratefully acknowledge the contributions of the study participants and dedication of the staff at the MWCCS sites.

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