Low-level viremia increases the risk of diabetes mellitus in people with HIV in China: a 7-year retrospective longitudinal cohort study

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Acknowledgement:
I would like to begin my presentation by expressing my deep gratitude to the people living with HIV who participated in this research. Our progress in the fight against HIV is made possible through the contributions and resilience of people living with HIV, both past and present.

Disclosure of interest:
The author(s) declare no conflicts of interest related to the content of this presentation.

CONTENTS

01

Background

Background

- As the life expectancy of people with HIV (PWH) increases, the risk of chronic diseases has risen dramatically, such as diabetes, hypertension, and dyslipidemia.
- Some individuals on ART experienced low-level viremia. Studies found that low-level viremia increases the risk of cardiovascular disease and metabolic syndrome.
- However, the specific impact of low-level viremia on the risk of developing DM remains uncertain.
- In this study, we explore the impact of low-level viremia (LV) on the development of diabetes mellitus (DM) among PWH using retrospective longitudinal cohort data.

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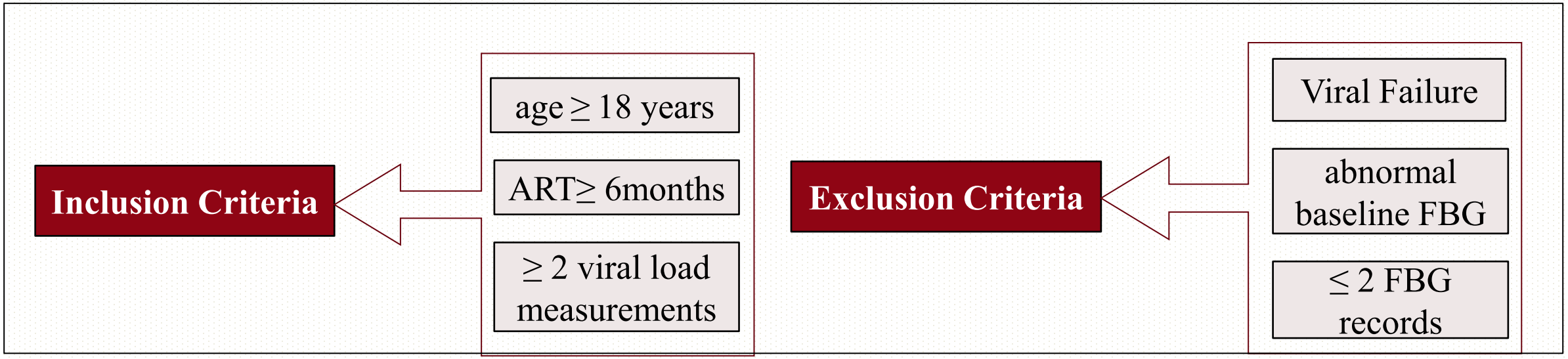
Methods

Study design and participants

- The data was extracted from China's National Free ART Program in Guangxi.
- PWH who started ART on or after January 2003, were included.



- Eligible participants were followed every 3 months until the incidence of DM, loss to follow-up (>180 days between FBG measurements), or administrative censoring, with a maximum observation of 7 years or until the cohort-wide deadline of October 2023.

Definitions of variables

	Primary Exposure: low-level viremia (LV)	
① Viral suppression (VS)	② Transient episode low-level viremia (blips)	③ Persistent low-level viremia (LLV)
All records of viral load were below 50 copies/mL.	one viral load 51-999 copies/mL, with tests before or after ≤50 copies/mL.	≥2 consecutive viral loads 51–199 copies/mL, ≥30 days apart, not meeting virologic failure (≥2 viral loads ≥200 or one ≥1000 copies/mL).

Outcome: diabetes mellitus (DM)
Two FBG ≥7.0 mmol/L, taken at least 30 days apart, and within 180 days.

Statistical methods

- Pearson's $\chi 2$ tests to compare baseline characteristics across the different enrollment viral load groups.
- Propensity score matching (PSM) to adjust for sex and age between the VS and LV groups.
- A trajectory analysis using heterogeneous linear mixed models was conducted to assess FBG changes over time and identify the different trajectories within each enrollment viral load group. The optimal number of groups was determined by synthesizing the Bayesian information criterion (BIC) and group size.
- Cox regression models to assess the risk of DM by enrollment viral load groups.

03

Results

Baseline characteristics

- Out of 42,196 participants, 8,731 were included in this study. Among them, the majority (7423, 85.0%) were classified into the VS group, the remaining 1308 (15.0%) were classified into the LV group.

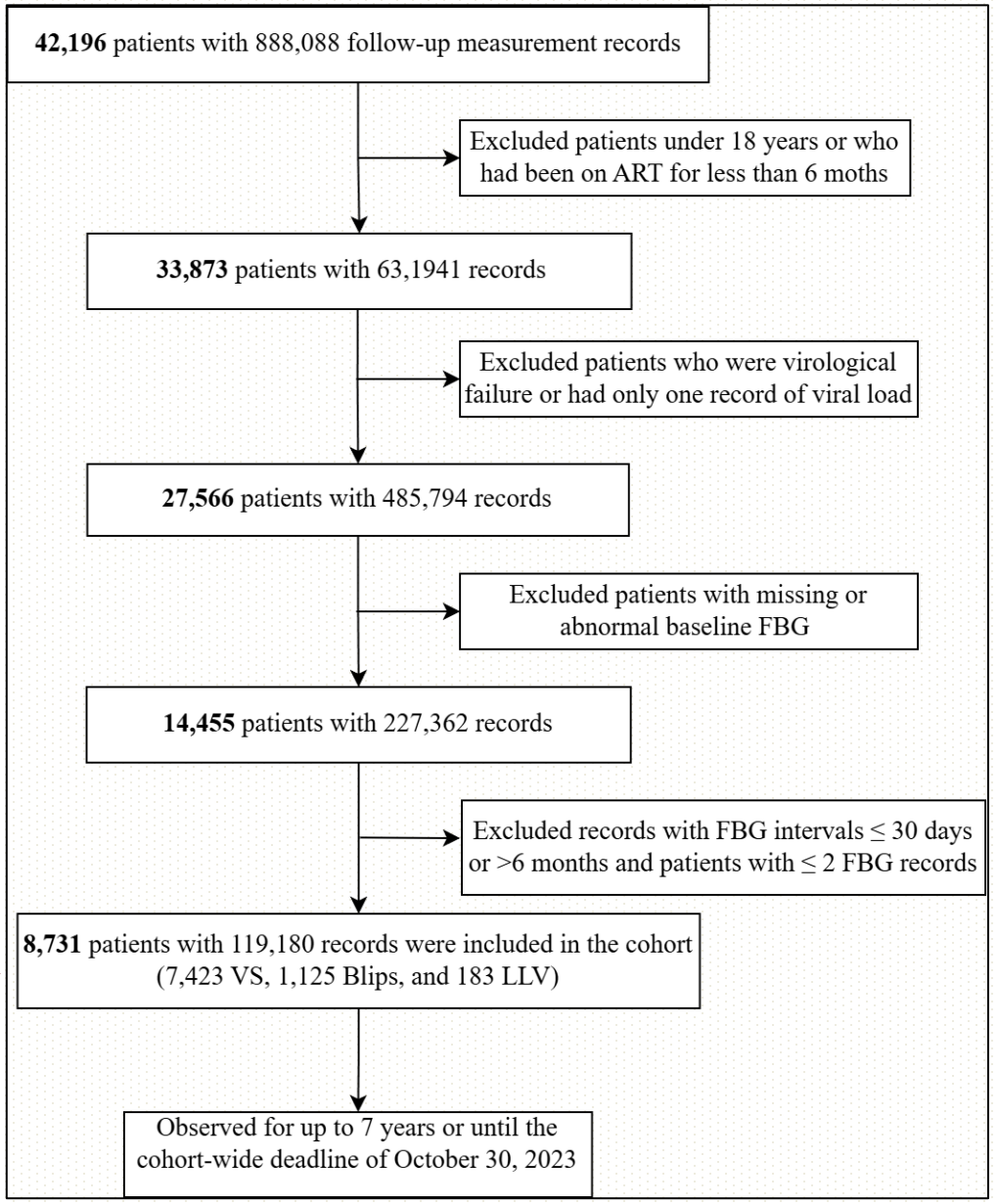


Fig.1. Exclusion flowchart of participants.

Figure 1

Baseline characteristics

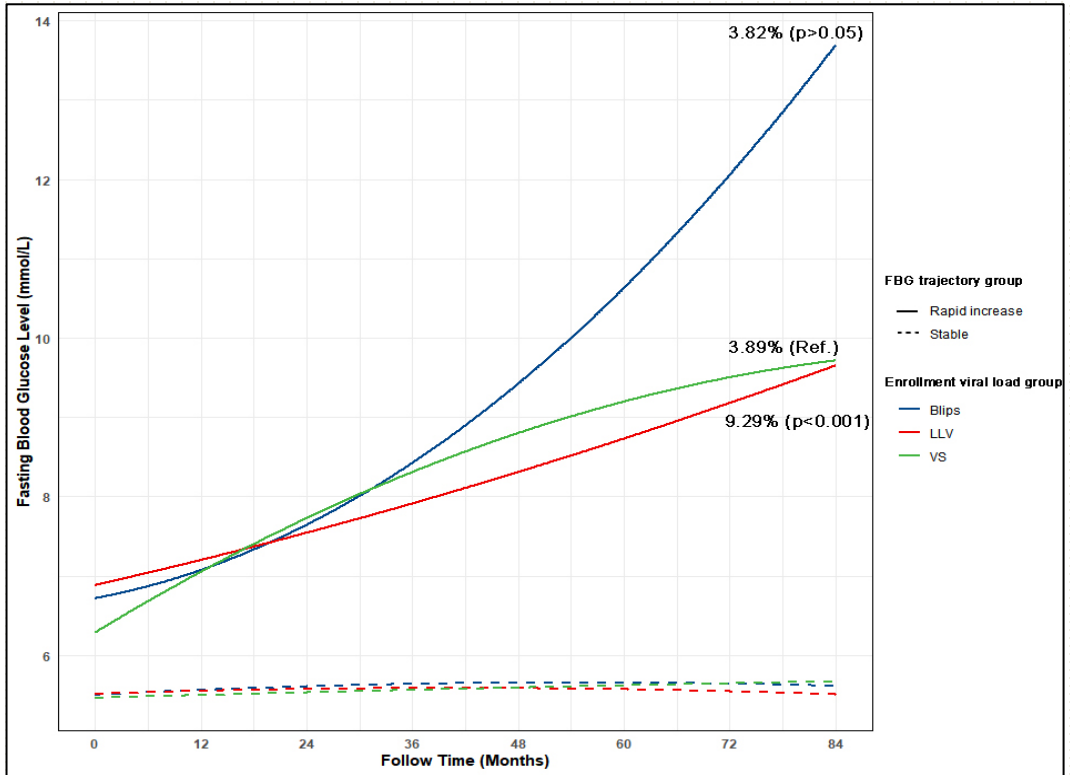
■ Socio-demographic and clinical characteristics

- Most participants were male (5949, 68.1%), married or partnered (5528, 63.3%), started ART before 2018 (6888, 78.9%), and with an EFV-based regimen (6172, 70.7%)
- The majority acquired HIV heterosexually (7289, 83.6%), and achieved viral suppression at baseline (5804, 66.5%).

Vars	Total	VS(n=7423)	blips (n=1125)	LLV (n=183)
Follow time (years, median [IQR])	2.4 [1.2, 4.5]	2.4 [1.2,4.6]	2.1 [1.1,4.2]	1.8 [1.0,3.6]
ART initiation period				
Before December 2018	6888 (78.9%)	5878 (79.2%)	864 (76.8%)	146 (79.8%)
After December 2018	1843 (21.1%)	1545 (20.8%)	261 (23.2%)	37 (20.2%)
ART initiation age (years)				
18-34	2686 (30.8%)	2361 (31.8%)	298 (26.5%)	27 (14.8%)
35-49	2696 (30.9%)	2344 (31.6%)	308 (27.4%)	44 (24%)
>=50	3349 (38.4%)	2718 (36.6%)	519 (46.1%)	112 (61.2%)
Sex				
Male	5949 (68.1%)	4998 (67.3%)	807 (71.7%)	144 (78.7%)
Female	2782 (31.9%)	2425 (32.7%)	318 (28.3%)	39 (21.3%)
Marital status				
Married/Partnered	5528 (63.3%)	4684 (63.1%)	728 (64.7%)	116 (63.4%)
Divorced/Widowed	1299 (14.9%)	1071 (14.4%)	194 (17.2%)	34 (18.6%)
Single	1904 (21.8%)	1668 (22.5%)	203 (18%)	33 (18%)
Transmission rout				
Heterosexual contact	7298 (83.6%)	6168 (83.1%)	973 (86.5%)	157 (85.8%)
Other or unkonwn	1433 (16.4%)	1255 (16.9%)	152 (13.5%)	26 (14.2%)
ART initial regimen				
EFV-based	6172 (70.7%)	5325 (71.7%)	734 (65.2%)	113 (61.7%)
NVP-based	1477 (16.9%)	1237 (16.7%)	217 (19.3%)	23 (12.6%)
PIs-based	993 (11.4%)	782 (10.5%)	167 (14.8%)	44 (24%)
INSTIs-based	89 (1.0%)	79 (1.1%)	7 (0.6%)	3 (1.6%)
Baseline viral load (copies/mL)				
<50	5804 (66.5%)	5386 (72.6%)	396 (35.2%)	22 (12%)
50-1000	1407 (16.1%)	762 (10.3%)	522 (46.4%)	123 (67.2%)
>=1000	1520 (17.4%)	1275 (17.2%)	207 (18.4%)	38 (20.8%)

FBG trajectory group

- Two distinct FBG trajectories were identified within each group (VS, blips, and LLV) using the growth mixture model (GMM).
- Individuals with a stable FBG trajectory were classified as the “Stable group”. Participants who experienced a marked increase in FBG were classified as the “Rapid Increase” group.

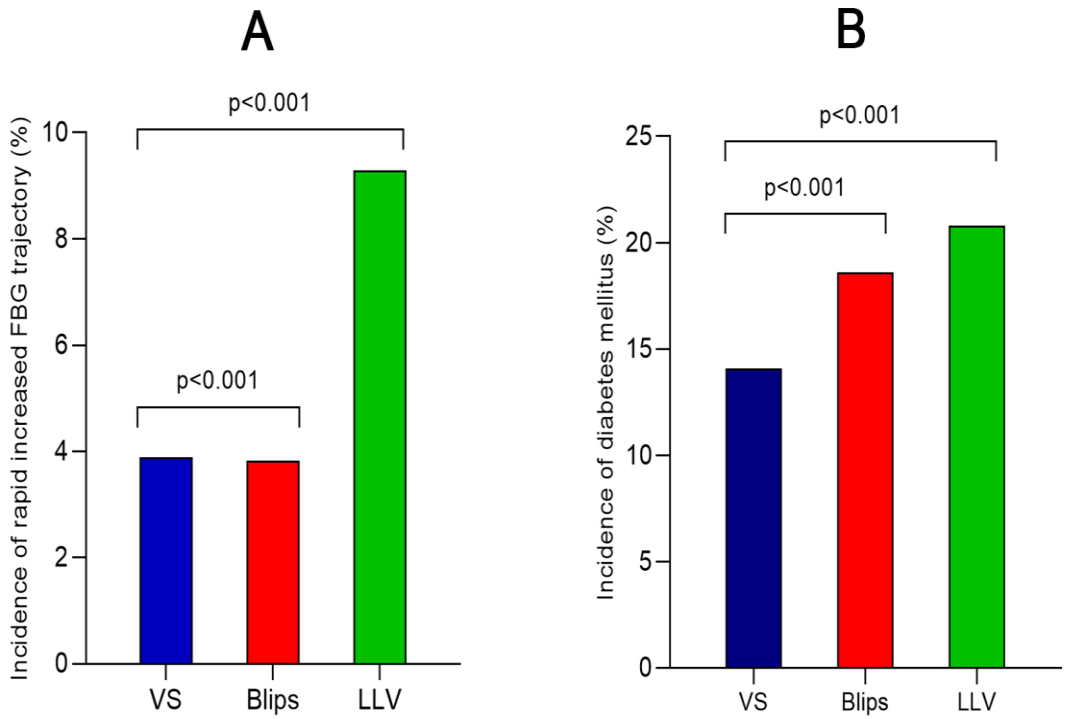


Enrollment viral load group	FBG trajectory group	Total	Month12	Month24	Month36	Month48	Month60	Month72	Month84
VS	Stable	7134	5957	4464	3349	2593	2005	1455	14
	Rapid increase	289	261	218	173	129	101	71	2
Blips	Stable	1082	36	31	23	19	14	11	0
	Rapid increase	43	888	650	488	368	274	205	0
LLV	Stable	166	136	97	70	48	36	27	1
	Rapid increase	17	16	13	10	8	4	4	0

Fig 2. FBG trajectories by viral load group

FBG rapid incread trajectory and DM incidence

- (A) A significantly higher proportion of participants in the LLV group followed the “Rapid Increase” FBG trajectory
- (B) Both blips and LLV groups had higher diabetes incidence than VS group, with LLV group showing the highest incidence.



Enrollment viral load group	Total	FBG rapid increase	OR(95%CI)	Diabetes mellitus	OR(95%CI)
VS	7423	289 (3.89%)		1050 (14.1%)	
Blips	1125	43 (3.82%)	0.98 (0.72-1.33)	209 (18.6%)	1.31(1.14,1.50)
LLV	183	17 (9.29%)	2.53 (1.53-4.16)	38 (20.8%)	1.47(1.10, 1.96)

Fig 3. Incidence of rapid increase FBG trajectory(A) and diabetes (B) across the three viral load groups

FBG trajectory group analysis

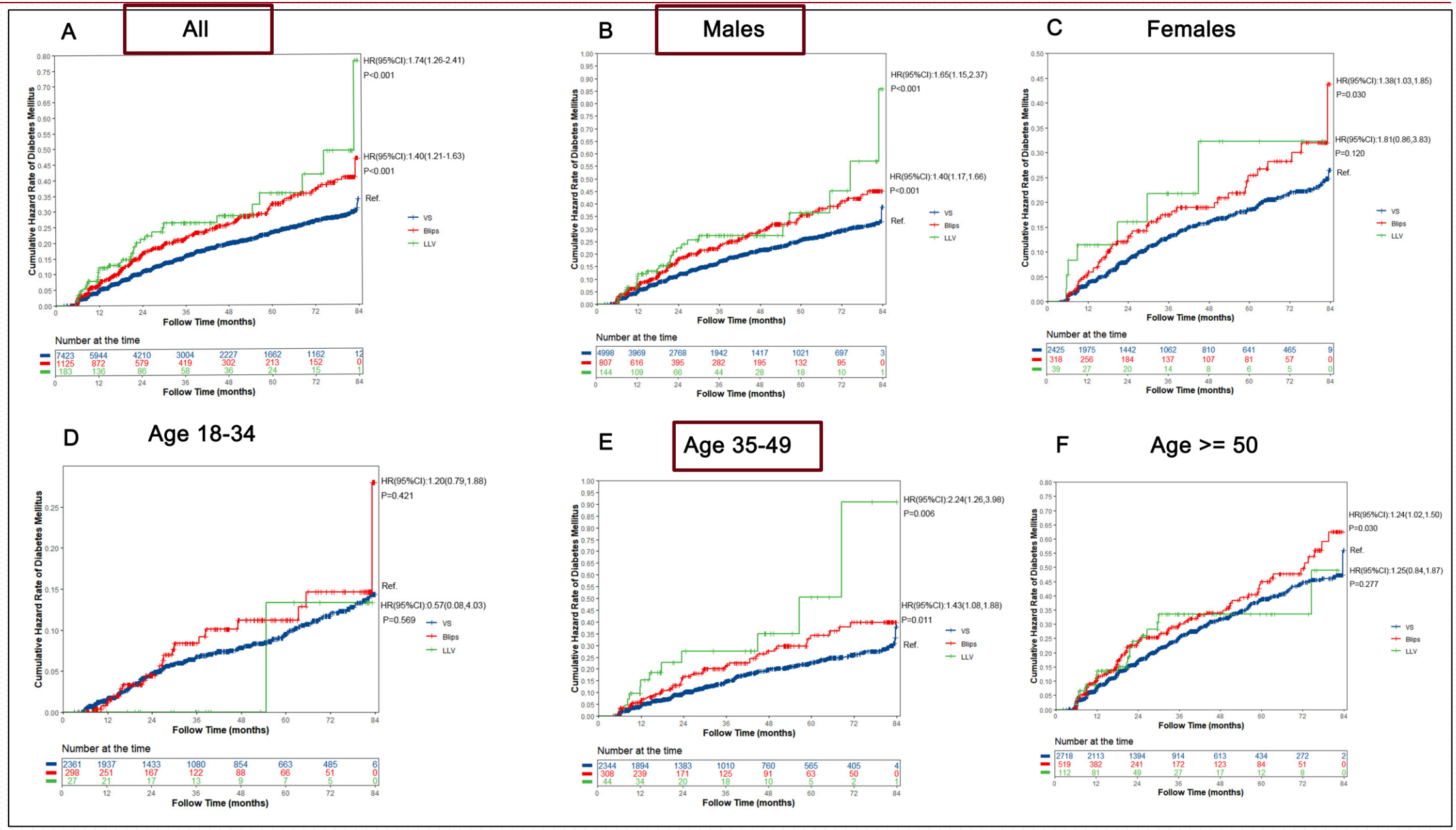


Figure 4

Table 3. Cox regression model for factors associated with DM

Vars	DM cases/Total (%)	cHR (univariable)	aHR (multivariable)	aHR (final)
Enrollment viral load groups				
VS	1050/7423 (14.1%)			
blips	209/1125 (18.6%)	1.40 (1.21-1.63, p<.001)	1.19 (1.02-1.40, p=.032)	1.23 (1.06-1.43, p=.006)
LLV	38/183 (20.8%)	1.74 (1.26-2.41, p<.001)	1.27 (0.90-1.78, p=.167)	1.33 (0.96-1.84, p=.089)
ART initiation period				
Before December 2018	1116/6888 (16.2%)			
After December 2018	181/1843 (9.8%)	1.45 (1.23-1.70, p<.001)	1.46 (1.23-1.74, p<.001)	1.42 (1.20-1.68, p<.001)
ART initiation age (years)				
18-34	181/2686 (6.7%)			
35-49	408/2696 (15.1%)	2.36 (1.98-2.81, p<.001)	2.18 (1.82-2.61, p<.001)	2.18 (1.82-2.61, p<.001)
>=50	708/3349 (21.1%)	3.86 (3.28-4.54, p<.001)	3.37 (2.81-4.04, p<.001)	3.37 (2.84-4.01, p<.001)
Sex				
Male	941/5949 (15.8%)			
Female	356/2782 (12.8%)	0.73 (0.65-0.83, p<.001)	0.72 (0.64-0.82, p<.001)	0.73 (0.64-0.82, p<.001)

Sensitivity analysis

Table 4. Association between viral load groups and DM, stratified by sex, age, ART initial period, and baseline WHO HIV stage.

Enrollment viral load groups	cHR(95%CI, p-value)	aHR(95%CI, p-value)
Stratified by age		
Age:18-34 (n=2686)		
VS		
Blips	1.20 (0.77-1.88, p=.421)	1.17 (0.75-1.83, p=.493)
LLV	0.56 (0.08-4.03, p=.569)	0.50 (0.07-3.58, p=.491)
Age:35-49 (n=2696)		
VS		
Blips	1.43 (1.08-1.88, p=.011)	1.36 (1.04-1.80, p=.027)
LLV	2.24 (1.26-3.98, p=.006)	2.03 (1.14-3.62, p=.017)
Age:>=50 (n=3349)		
VS		
Blips	1.24 (1.02-1.50, p=.030)	1.23 (1.02-1.49, p=.034)
LLV	1.25 (0.84-1.86, p=.277)	1.23 (1.02-1.49, p=.034)
Stratified by ART initiation period		
Before December 2018 (n=6888)		
VS		
Blips	1.37 (1.16-1.61, p<.001)	1.24 (1.05-1.46, p=.010)
LLV	1.90 (1.36-2.67, p<.001)	1.49 (1.06-2.09, p=.022)
After December 2018 (n=1843)		
VS		
Blips	1.54 (1.07-2.21, p=.019)	1.45 (1.01-2.09, p=.044)
LLV	0.85 (0.27-2.66, p=.779)	0.75 (0.24-2.36, p=.627)
Stratified by baseline WHO HIV stage		
Stage I~II (n=5243)		
VS		
Blips	1.44 (1.18-1.77, p<.001)	1.25 (1.02-1.53, p=.034)
LLV	1.17 (0.66-2.07, p=.590)	0.93 (0.52-1.65, p=.804)
Stage III~IV(n=3488)		
VS		
Blips	1.34 (1.08-1.67, p=.009)	1.29 (1.04-1.61, p=.022)
LLV	2.19 (1.47-3.25, p<.001)	1.82 (1.22-2.71, p=.003)

- Among individuals aged 35-49 years, those starting ART before December 2018, and those with baseline WHO stage III–IV, both the blips and LLV groups were significantly associated with an increased risk of DM.

Table 5. Cox regression model for factors associated with DM after matching for age and sex

Vars	DM cases/Total (%)	cHR (univariable)	aHR (multivariable)	aHR (final)
Enrollment viral load groups				
VS	204/1308 (15.6%)			
LV	247/1308 (18.9%)	1.26 (1.05-1.52, p=.015)	1.18 (0.96-1.46, p=.118)	1.27 (1.05-1.53, p=.012)
ART initiation period				
Before December 2018	381/2021 (18.9%)			
After December 2018	70/595 (11.8%)	1.39 (1.07-1.81, p=.015)	1.37 (1.05-1.79, p=.021)	1.37 (1.05-1.78, p=.021)
ART initiation age (years)				
18-34	48/650 (7.4%)			
35-49	115/704 (16.3%)	2.33 (1.66-3.26, p<.001)	2.17 (1.54-3.07, p<.001)	2.30 (1.64-3.22, p<.001)
>=50	288/1262 (22.8%)	3.76 (2.77-5.10, p<.001)	3.53 (2.53-4.93, p<.001)	3.77 (2.77-5.12, p<.001)
Sex				
Male	339/1902 (17.8%)			
Female	112/714 (15.7%)	0.79 (0.64-0.98, p=.031)	0.81 (0.64-1.01, p=.058)	0.79 (0.64-0.98, p=.029)

Sensitivity analysis

Table 6. Association between viral load groups and DM, after matching for sex and age, stratified by sex, age, ART initial period, and baseline WHO HIV stage.

	Enrollment viral load groups	cHR(95%CI)	p-value
Stratified by sex			
Male (n=1902)			
	VS	Ref.	
	LV	1.31(1.05,1.62)	p=0.015
Female (n=714)			
	VS	Ref.	
	LV	1.14(0.78,1.65)	p=0.497
Stratified by age			
Age:18-34 (n=650)			
	VS	Ref.	
	LV	0.99(1.01,1.75)	p=0.979
Age:35-49 (n=704)			
	VS	Ref.	
	LV	1.72(1.18,2.51)	p=0.005
Age:>=50 (n=1262)			
	VS	Ref.	
	LV	1.16(0.92,1.46)	p=0.208
Stratified by ART initiation period			
Before December 2018 (n=2021)			
	VS	Ref.	
	LV	1.25 (1.03-1.54)	p=.027
After December 2018 (n=595)			
	VS	Ref.	
	LV	1.25 (0.78-2.02)	p=.348
Stratified by baseline WHO HIV stage			
Stage I~II (n=1506)			
	VS	Ref.	
	LV	1.27 (0.99-1.65)	p=.064
Stage III~IV (n=1110)			
	VS	Ref.	
	LV	1.22 (0.93-1.60)	p=.149

- The association between LV and DM remained significant in males, individuals aged 35-49 years, and those who initiated ART before December 2018.

Summary

1. Low-level viremia is significantly associated with the development of diabetes mellitus (DM) among PWH, particularly in middle-aged individuals.

2. Proactive monitoring of viral load and fasting blood glucose (FBG) is essential to prevent the development of DM and to extend the life expectancy, especially for the middle age and the advanced WHO HIV stage group.

Tao C, Wei L, Liang B, et al. Low-level viremia increases the risk of diabetes mellitus in people with HIV in China: a 7-year retrospective longitudinal cohort study. BMC Medicine. 2025 Jul 1;23(1):350. PMID: 40597125

There are more than 100,000 people living with HIV in Guangxi Province, with approximately 10,000 HIV newly reported cases every year. Most of the newly reported cases are older adults. So, we have a large cohort. I hope that research teams interested in studying the cohort of HIV patients with chronic diseases can collaborate with us.

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Research Interest:

- HIV/STI associated Innovative prevention;
- HIV treatment cohort;
- HIV molecular epidemiology;
- Sexual Health.

Grants:

- HIV-1 Transmission Among Older Males/MSM in Guangxi (2022-2024);
- Social and Genetic Networks of HIV-1 in China-Vietnam (2021-2024);
- Precise HIV Prvention Based on Transmission Networks (RCT) (2023-2025);
- HIV Treatment Cohort (2022-2025).

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THANK YOU!

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