

# Suboptimal Immune Recovery Despite Sustained HIV Suppression Among a Yi Ethnic Population in Southwest China

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## Research Article

**Keywords:** HIV-infected Yi ethnic population, sustained HIV suppression, immune recovery

**Posted Date:** June 18th, 2021

**DOI:** <https://doi.org/10.21203/rs.3.rs-604340/v1>

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## Abstract

**Objectives:** Despite sustained viral suppression with effective antiretroviral therapy (ART), HIV-infected patients with suboptimal immune recovery are still at high risk of non-AIDS-related and AIDS-related events. The aim of this study was to investigate the potential determinants associated with suboptimal CD4+ T cell count recovery during free ART with sustained viral suppression among a HIV-infected Yi ethnic population in Liangshan Prefecture, an area with high HIV prevalence in China.

**Method:** This retrospective study included all HIV-infected Yi adults ( $\geq 18$  years and with baseline CD4+ T cell count less than 500 cells/ $\mu$ L) who initiated ART supported by NFATP between January 2015 and December 2018 in Zhaojue county, Liangshan Prefecture (Figure 1), and achieved virological suppression (viral load  $< 50$  copies/mL) within 12 months after ART initiation and maintained sustained virological suppression. Univariate and multivariate log-binomial regression models were used to assess determinants of suboptimal immune recovery, producing adjusted odds ratios (aORs) and confidence intervals (CIs).

**Results:** A total of 277 HIV-infected Yi patients (male/female, 140/137) with a mean age of  $36.57 \pm 7.63$  years and a mean baseline CD4+ T cell count of  $284.49 \pm 117.11$  cells/ $\mu$ L were included. Nearly half of the Yi patients were infected through injection drug use (48.7%, 135/277), and the prevalence of anti-HCV antibody was high (43.7%, 121/277). The free ART regimens were 91% efavirenz-based, 5.1% nevirapine-based, and 3.9% lopinavir/ritonavir-based. After a mean  $3.77 \pm 1.21$  years of ART, optimal immune recovery (CD4+ T cell count  $\geq 500$  cells/ $\mu$ L), intermediate immune recovery ( $350 \leq \text{CD4} < 500$  cells/ $\mu$ L), and suboptimal immune recovery ( $\text{CD4} < 350$  cells/ $\mu$ L) occurred in 32.9%, 31%, and 36.2% of the included patients, respectively. After adjustments, multivariable analysis revealed that low pre-ART CD4+ cell count, WHO clinical stage III and IV, and coinfection with HCV were associated with suboptimal immune recovery.

**Conclusions:** Our study support prompt ART initiation after HIV diagnosis, and curative HCV treatment in HCV/HIV co-infected patients for improving the immunological effectiveness of ART among HIV-infected Yi patients in Liangshan Prefecture.

**Trial registration:** None

## Introduction

HIV/AIDS has been one of the world's most serious public health challenges since its first report in 1981 (1). According to United Nations Program on HIV/AIDS (UNAIDS), there were 38.0 million people (36.2 million adults, 1.8 million children) globally living with HIV/AIDS in 2019. Of these, 1.7 million were newly infected in 2019 (<https://www.unaids.org/en>). By the end of 2020, the number of people living with HIV in China surpassed 1 million, of which more than 12,000 people were the newly infected (<http://www.nhc.gov.cn/wjw/>). Although the overall national prevalence of HIV/AIDS in China remains low, the prevalence varies greatly in different regions and among different ethnic populations.

Liangshan Yi Autonomous Prefecture with 53.84% of its population consisted of Yi ethnic people (approximately 2.86 million), located in Sichuan province, southwest of China, is a high epidemic area. Currently, all the six counties (Butuo, Zhaojue, Meigu, Yuexi, Jinyang and Puge) in China with HIV/AIDS prevalence surpassing 1% are located within Liangshan prefecture. Most of the HIV-infected cases in Liangshan Prefecture are Yi people, and the dominant transmission routes are injection drug use (IDU) and heterosexual contact (2–4). The high prevalence of HIV infection among the Yi population can be partly ascribed to Liangshan prefecture's geographical location and Yi people's cultures. On the border with Yunnan province, Liangshan prefecture has long been an important channel for drug smuggling from the Golden Triangle into Sichuan Province, and the use of heroin has even been socially acceptable among the Yi people (2, 3). In addition, poverty, casual sex including extramarital sex and concurrent sexual partnerships are also risk factors for the high HIV prevalence in this region.

To effectively control the HIV/AIDS epidemic in Liangshan prefecture, China's National Free Antiretroviral Treatment Program (NFATP) provides free anti-retroviral therapy (ART) to all people living with HIV in the area. Of note, integrase inhibitors have not been included in NFATP, and thus most of the ART regimens provided by the NFATP are non-nucleoside reverse transcriptase inhibitor (NNRTI)-based or protease inhibitor-based. Through the widespread implementation of the ART, the percentage of patients having access to ART keeps increasing, enabling more and more HIV/AIDS patients achieve and maintain an undetectable viral load. Since the Undetectable equals Untransmissible (5), the NFATP in Liangshan Prefecture has made a great contribution to the effective control of HIV transmission. However, we have observed a considerable proportion of HIV-infected Yi patients fail to achieve CD4 + T cell recovery to a normal level ( $\geq 500$  cells/ $\mu\text{L}$ ) despite they have achieved and maintained a sustained HIV suppression. These patients with suboptimal immune recovery are still at high risk of non-AIDS-related and AIDS-related events. To further improve the ART efficacy, the aim of this study was to investigate the potential determinants associated with suboptimal CD4 + count recovery in HIV-infected Yi people who have achieved sustained viral suppression under China's NFATP in Zhaojue county, Liangshan Prefecture.

## Materials And Methods

### Study design and patients

This retrospective study included all HIV-infected Yi adults ( $\geq 18$  years and with baseline CD4+ T cell count less than 500 cells/ $\mu\text{L}$ ) who initiated ART supported by NFATP between January 2015 and December 2018 in Zhaojue county, Liangshan Prefecture (Figure 1), and achieved virological suppression (viral load  $< 50$  copies/mL) within 12 months after ART initiation and maintained sustained virological suppression. Based on a recent study (6), patients' immune recovery was stratified by CD4+ T cell count measured at the latest follow-up visit to complete immune recovery (CD4  $\geq 500$  cells/ $\mu\text{L}$ ); intermediate immune recovery ( $350 \leq \text{CD4} < 500$  cells/ $\mu\text{L}$ ); and suboptimal immune recovery (CD4  $< 350$  cells/ $\mu\text{L}$ ). Of note, all the HIV-infected Yi patients in this study were from Zhaojue county of Liangshan Prefecture. As the integrase inhibitors have not been included in NFATP, the current first-line NFATP ART regimen was consisted of NNRTI: efavirenz (EFV) or nevirapine (NVP), or a protease inhibitor: lopinavir/

ritonavir (LPV/r) in combination with tenofovir disoproxil fumarate (TDF) /lamivudine (3TC) or Zidovudine (AZT)/3TC.

CD4+ T cell count was measured using flow cytometry (BD-FACSCalibur), and HIV-RNA in plasma was measured using the Roche Cobas TaqMan HIV-1 (HPS) test every 12 months till the end of 2020. Thus, the longest follow-up time was 72 months and the shortest follow-up time was 24 months. Anti-hepatitis C virus (HCV) antibodies, and hepatitis B surface antigen (HBsAg) were measured by the HCV antibody kit and the HBsAg test kit, respectively (KHB, China). In addition, other routine follow-up tests including hematology, urinalysis and blood liver function were measured every 6 months; renal function for patients taking TDF, and serum lipid for patients taking LPV/r measured every 6 months. This study was approved by the Medical Ethics Committee of West China Hospital of Sichuan University (Annual Audit No. 450, Version 2020.5). The study was performed by following the ethical guidelines expressed in the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice. Informed consent was obtained from all subjects.

## Statistics

Data were extracted from the NFATP Data System. Data were reported as the mean  $\pm$  standard deviation for normal continuous variables and median (interquartile range) for non-normal continuous variables, while frequency was used for discrete variables. Univariate and multivariate log-binomial regression models were used to assess determinants of suboptimal immune recovery, producing adjusted odds ratios (aORs) and confidence intervals (CIs). Confounders or predictors for each outcome were analyzed as covariates according to their biologically plausible. Variance inflation factor (VIF) and tolerance (1/VIF) values were used for checking the collinearity between factors included in the multivariable analysis. All  $p$ -values were 2-sided, and  $p < 0.05$  was considered statistically significant. Statistical analyses were performed using statistical software SPSS (Version 24.0, IBM, Armonk, New York, US).

## Results

Between January 2015 and December 2018, 277 HIV-infected Yi patients (with baseline CD4 + T cell count less than 500 cells/ $\mu$ L) who initiated ART and achieved sustained virological suppression were included in this study to investigate the incidence of suboptimal immune recovery and the associated determinants (Fig. 2). There were 140 female and 137 male patients in this study with a mean age of  $36.57 \pm 7.63$  years (Table 1). Most of the Yi patients were infected through injection drug use (IDU) (48.7%) and heterosexual contact (49.8%). Of note, the prevalence of anti-HCV antibody and HBsAg positivity among these patients was high, being 43.7% (121/277) and 11.9% (33/277), respectively. At ART initiation, the baseline mean HIV viral load was  $5.16 \pm 0.22 \log_{10}$  copies/ml. The mean baseline CD4 + T cell count was  $284.49 \pm 117.11$  cells/ $\mu$ L, and the proportion of patients with CD4 + T cell count  $< 100$ , 100–200, 200–350, 350–500 cells/ $\mu$ L was 4% (11/277), 23.1% (64/277), 41.5% (115/277), and 31.4 % (87/277), respectively. Most of the included Yi patients were in WHO clinical stage I and II (269/277,

97.1%), whereas only 8 patients (2.9%) were in stage III and IV. The ART regimens were based on efavirenz (EFV) (91%, 251/277), NVP (5.1%, 14/277), or LPV/r (3.9%, 11/277) in combination with TDF/3TC or AZT/3TC (Table 1).

**Table 1**  
**Patients' characteristics at ART initiation**

<b>Variables</b>	<b>Patients (n = 277)</b>
Sex	
Female (%)	140 (50.5%)
Male (%)	137 (49.5%)
Age (years)	36.57 ± 7.63
CD4 + T cell count (cells/µL)	284.49 ± 117.11
HIV viral load ( $\log_{10}$ copies/mL)	5.16 ± 0.22
BMI (kg/m <sup>2</sup> )	
<18.5	47 (17.0%)
18-24.5	193 (69.7%)
>24.5	37 (13.4%)
Hemoglobin (g/dL)	145.88 ± 123.86
HBsAg positivity (%)	33 (11.9%)
Anti-HCV positivity (%)	121 (43.7%)
WHO stage (%)	
I and II	269 (97.1%)
III and IV	8 (2.9%)
ART regimens (%)	
AZT + 3TC + LPV/r	9 (3.2%)
AZT + 3TC + EFV	72 (26.4%)
AZT + 3TC + NVP	11 (4.0%)
TDF + 3TC + LPV/r	2 (0.7%)
TDF + 3TC + EFV	179 (64.6%)
TDF + 3TC + NVP	3 (1.1%)
Treatment duration (years)	3.77 ± 1.21

AZT, zidovudine; 3TC, lamivudine; LPV/r, Lopinavir/ ritonavir; EFV, efavirenz; NVP, nevirapine; TDF, tenofovir disoproxil fumarate.

During the follow-up period, the proportion of patients with CD4 + T cell count  $\geq$  350 cells/ $\mu$ L increased from 31.4% (87/277) to 63.9% (177/277), and with CD4 + T cell count  $\geq$  200 cells/ $\mu$ L increased from 72.9% (202/277) to 90.3% (250/277) (Fig. 3). However, Of the 277 patients with a mean  $3.77 \pm 1.21$  years of ART, optimal or complete immune recovery (CD4 + T cell count  $\geq$  500 cells/ $\mu$ L), intermediate immune recovery ( $350 \leq$  CD4 < 500 cells/ $\mu$ L) occurred in 32.9% and 31% of the included patients, whereas suboptimal immune recovery with CD4 + T cell counts less than 350 cells/ $\mu$ L occurred in 36.2% of the included patients (Fig. 3).

To further investigate the potential determinants associated with suboptimal CD4 + count recovery among this population, multivariable analysis was carried out. We demonstrated that low pre-ART CD4 + cell count, WHO clinical stage III and IV, and coinfection with HCV were associated with suboptimal immune recovery. Specifically, compared with patients having a pre-ART CD4 + cell count  $\geq$  350 cells/ $\mu$ L, patients with pre-ART CD4 + cell count in the range of 200–350 cells/ $\mu$ L (aOR 0.353, 95% CI 0.187–0.666,  $p = 0.001$ ), and 100–200 cells/ $\mu$ L (aOR 0.432, 95% CI 0.211–0.885,  $p = 0.022$ ) had a lower chance to achieve a CD4 + T cell count  $\geq$  500 cells/ $\mu$ L (Table 2). However, pre-ART CD4 + cell count < 100 cells/ $\mu$ L was not found to be associated with immune recovery, which might be ascribed with the very small number of patients (only 11) having a pre-ART CD4 + cell count < 100 cells/ $\mu$ L in this study. Patients in WHO clinical stage III and IV had a lower chance likely to achieve a CD4 + T cell count  $\geq$  200 cells/ $\mu$ L than patients in WHO clinical stage I and II (aOR 0.104, 95% CI 0.012–0.909,  $p = 0.041$ ). Interestingly, coinfection with HCV was found to be associated with lower chance to achieve a CD4 + T cell count  $\geq$  200 cells/ $\mu$ L (aOR 0.261, 95% CI 0.095–0.716,  $p = 0.009$ ), and  $\geq$  350 cells/ $\mu$ L (aOR 0.500, 95% CI 0.281–0.891,  $p = 0.019$ ). Age, sex, BMI, baseline viral load, anemia, treatment duration, and coinfection with HBV were not found to be associated with immune recovery in this study.

Table 2

Determinants associated with suboptimal CD4 + count recovery among Yi patients with sustained HIV suppression on ART

	CD4 + cell count > 200 cells/ $\mu$ L		CD4 + cell count > 350 cells/ $\mu$ L		CD4 + cell count > 500 cells/ $\mu$ L	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
<b>Age (years)</b>						
18–29	Reference		Reference		Reference	
30–39	1.004 (0.272–3.714)	0.995	0.657 (0.311–1.389)	0.272	0.946 (0.475–1.887)	0.875
40–49	0.947 (0.227–3.961)	0.941	0.594 (0.261–1.349)	0.213	0.637 (0.287–1.412)	0.267
≥50	0.856 (0.073–9.972)	0.901	0.421 (0.113–1.573)	0.198	0.820 (0.210–3.195)	0.775
Male sex	0.499 (0.179–1.388)	0.183	0.849 (0.470–1.534)	0.588	0.590 (0.325–1.073)	0.084
<b>Pre-ART CD4 + count atsta(cells/ml)</b>						
<100	0.650 (0.092–4.576)	0.665	0.960 (0.246–3.745)	0.953	0.348 (0.082–1.474)	0.152
100–199	Reference		0.642 (0.333–1.237)	0.185	0.432 (0.211–0.885)	0.022
200–350			Reference		0.353 (0.187–0.666)	0.001
350–500					Reference	
<b>BMI (kg/m<sup>2</sup>)</b>						
<18.5	1.276 (0.402–4.053)	0.679	0.565 (0.280–1.140)	0.111	0.904 (0.428–1.912)	0.792
18.5–24	Reference		Reference		Reference	
>28	4.413 (0.528–36.858)	0.170	1.180 (0.517–2.694)	0.695	0.887 (0.389–2.021)	0.775

	CD4 + cell count > 200 cells/ $\mu$ L	CD4 + cell count > 350 cells/ $\mu$ L	CD4 + cell count > 500 cells/ $\mu$ L			
<b>HIV viral load (copies/mL)</b>						
<100 000	Reference	Reference	Reference			
>100 000	1.123 (0.377–3.345)	0.835	0.670 (0.337–1.330)	0.252	0.967 (0.499–1.874)	0.920
<b>WHO clinical stage</b>						
I and II	Reference	Reference	Reference			
III and IV	0.104 (0.012–0.909)	0.041	0.634 (0.140–2.875)	0.554	1.628 (0.346–7.662)	0.537
Anemia	0.494 (0.134–1.818)	0.289	0.740 (0.314–1.746)	0.492	0.766 (0.306–1.918)	0.569
Treatment duration > 3 years	0.618 (0.230–1.656)	0.338	0.596 (0.333–1.066)	0.081	0.980 (0.557–1.725)	0.944
HBsAg positivity	5.244 (0.573–47.957)	0.142	1.433 (0.597–3.441)	0.420	1.195 (0.534–2.677)	0.665
Anti-HCV positivity	0.261 (0.095–0.716)	0.009	0.500 (0.281–0.891)	0.019	0.734 (0.405–1.331)	0.309

## Discussion

With the advent of ART, HIV infection has been transformed from a death sentence to a chronic but treatable disease for most of the HIV-infected individuals. However, around 30% of ART-receiving patients fail to exhibit CD4 + T cell recovery to a normal level despite achieving a sustained HIV suppression (7, 8). Persistently low CD4 + T cell counts are associated with an increased risk of both AIDS-related and non-AIDS-related morbidity and mortality (9). Thus, identification of all the possible risk factors involved in poor CD4 + T cell recovery may provide clinicians guidance in choosing the most effective treatment approaches for these critical patients (8). In the present study, of the 277 HIV-infected Chinese Yi ethnic patients evaluated after a mean  $3.77 \pm 1.21$  years of ART, we demonstrated that only 32.9% patients achieved optimal immune recovery with the CD4 + T cell count  $\geq 500$  cells/ $\mu$ L at the last follow-up visit, whereas the suboptimal immune recovery at CD4 + T cell counts less than 200 cells/ $\mu$ L, and less than 350 cells/ $\mu$ L occurred in 9.8%, and 36.2% of the included patients, respectively.

To our knowledge, this is the first study to analyze the risk factors potentially associated with suboptimal immune recovery among HIV-infected Yi ethnic patients in Liangshan Prefecture, Southwest China. Through multivariable logistic regression analysis, we demonstrated that low pre-ART CD4 + cell count is an independent risk factor for suboptimal immune recovery, which is consistent with previous studies (6, 8, 10, 11). Compared with patients having baseline CD4 + cell count  $\geq$  350 cells/ $\mu$ L, patients with baseline CD4 + cell count between 200 and 350 cells/ $\mu$ L, and between 100 and 200 cells/ $\mu$ L at ART initiation are more likely to have suboptimal immune recovery (Table 2). This is consistent with previous studies showing that many individuals who start ART at CD4 + cell count  $<$  350 cells/ $\mu$ L never achieve a normal CD4 + cell count  $\geq$  500 cells/ $\mu$ L even after up to 10 years of effective ART (11, 12). In addition, compared with patients in WHO clinical stage I and II, patients in WHO clinical stage III and IV are less likely to achieve a CD4 T cell count  $\geq$  200 cells/ $\mu$ L (Table 2). The above results corroborate the current international guideline recommending that prompt or even immediate ART initiation on the day of HIV diagnosis is of great importance to individuals living with HIV before they have markedly declined CD4 + T cell counts and progressed to AIDS (13).

In the present study, the prevalence of HBV/HIV coinfection was 11.9%, which was comparable to the HBV/HIV coinfection rate (13.85%) recently reported among HIV-infected patients in Guangxi Zhuang Autonomous region (14). The HBV infection rate among the HIV-infected individuals is much higher than that of the general population (5–6%) in China (15). Consistent with previous studies (16–18), our study revealed that HBV status did not influence CD4 + T cell response upon ART initiation (Table 2). However, it needs to emphasize that the progression of chronic HBV infection to severe end-stage liver diseases including liver failure, cirrhosis, and hepatocellular carcinoma is more rapid in individuals with HBV/HIV coinfection than in individuals with HBV mono-infection (9, 19). Thus, in patients with HBV/HIV coinfections, TDF or TAF in combination with FTC should be the ART backbone because these three drugs are active against both viruses (9, 13). The ART backbone used in this study was mostly TDF/3TC (66.4%) with the remaining 33.6% being AZT/3TC (Table 1). It is expected that the ART backbone AZT/3TC will be gradually removed from China NFATP and replaced by TDF/emtricitabine (FTC).

The prevalence of positive anti-HCV antibody among the included 277 HIV-infected Yi patients in this study was 43.7%, which could be explained by the fact that 48.7% of the patients were infected through injection drug use. Both HCV and HIV are blood-borne viruses, and the presence of HIV infection increases the transmission efficiency of HCV (20). It has been reported that HCV prevalence in HIV-infected individuals is much higher than HIV-negative individuals, especially in people who inject drugs (82·4%, 55·2–88·5) (20). HIV co-infection accelerates HCV progression as patients with HCV/HIV coinfection had a 2.92-fold greater risk of progression to severe liver diseases than patients with HCV mono-infection (21). However, the effect of HCV infection on CD4 + T cell recovery after efficient ART remains controversial. Some studies reported that the CD4 + T cell recovery was comparable between HCV/HIV co-infected patients and HIV-mono-infected patients on efficient ART (22), or that the clearance of HCV replication did not influence immune recovery (23). On the contrary, several studies found that despite sustained HIV suppression on efficient ART, HCV/HIV co-infected patients had lower probability to achieve optimal immune recovery as compared with patients with HIV mono-infection (24–28). Our present study

also revealed a negative correlation between HCV infection and the optimal CD4 + T cell recovery (Table 2), suggesting that all patients with HCV/HIV co-infection should be evaluated for curative HCV treatment (9). With the advent of direct-acting antiviral (DAA) therapies, HIV/HCV co-infection is no longer a difficult to treat population (29). Of note, when concurrent treatments for both HIV and HCV are indicated, careful consideration needs to be taken for drug-drug interactions between ART drugs and HCV DAs. In the present study, more than 95% of the ART regimens are EFV and NVP-based (Table 1), the DAA regimen sofosbuvir/ledipasvir is recommended for HCV eradication, whereas the DAA regimens including sofosbuvir/velpatasvir, elbasvir/grazoprevir, and glecaprevir/pibrentasvir are contraindicated. As velpatasvir, elbasvir, grazoprevir, and glecaprevir are substrates of cytochrome P450 3A (CYP3A), their serum concentrations will be reduced when co-administrated with EFV and NVP (the CYP3A inducers) (9, 30).

Our study has limitations. First, all the included patients were on NNRTI-based or protease inhibitor-based ART regimens, precluding the assessment of immune recovery in patients on integrase-based ART regimens. Second, HCV-RNA levels were not measured in this study, and therefore patients with positive anti-HCV antibody but negative HCV RNA viral load may be included. Third, the number of Yi patients on efficient ART but with suboptimal immune recovery included in this study was relatively small, which may limit the identification of other determinants associated with suboptimal CD4 + T cell count recovery. Future studies are needed to include more Yi patients from Liangshan Prefecture to investigate more factors (e.g., age, gender, BMI, alcohol consumption, CD4+/CD8 + T cell counts ratio, CD8 + T cell counts, and ART regimens) that are likely to influence immune recovery of HIV-infected patients on efficient ART (8, 10, 31, 32).

In summary, we demonstrated that low pre-ART CD4 + cell count and HCV infection were associated with suboptimal CD4 + count recovery among HIV-infected Yi people on efficient ART in Liangshan Prefecture. Our study support prompt ART initiation after HIV diagnosis, and the HCV eradication treatment in HCV/HIV co-infected patients by appropriate DAA regimens (compatible with HIV ART antiretrovirals) not only for HCV cure *per se* but also for improving the immunological effectiveness of ART.

## Strength And Limitations Of This Study

1. This was a retrospective study including 277 HIV-infected Yi ethnic patients with sustained viral suppression in Liangshan Prefecture (an area with the highest HIV prevalence in China) to investigate the potential determinants associated with suboptimal CD4+ T cell count recovery
2. All the included patients were on NNRTI-based or protease inhibitor-based ART regimens, precluding the assessment of immune recovery in patients on integrase-based ART regimens
3. HCV-RNA levels were not measured in this study, and therefore patients with positive anti-HCV antibody but negative HCV RNA viral load may be included.

## **Abbreviations**

UNAIDS: United Nations Program on HIV/AIDS;

IDU: injection drug use;

ART: anti-retroviral therapy;

NFATP: National Free Antiretroviral Treatment Program

NNRTI: non-nucleoside reverse transcriptase inhibitor;

EFV: efavirenz;

NVP: nevirapine;

LPV/r: lopinavir/ ritonavir;

TDF: tenofovir disoproxil fumarate;

3TC: lamivudine;

AZT: Zidovudine;

HCV: anti-hepatitis C virus;

HBV: hepatitis B surface antigen;

aORs: adjusted odds ratios;

CIs: confidence intervals;

VIF: Variance inflation factor;

CYP3A: cytochrome P450 3A.

## **Declarations**

### **Ethics approval and consent to participate:**

Yes, this study was approved by the Medical Ethics Committee of West China Hospital of Sichuan University (No. 450, Version 2020.5) (in related files). The study was performed by following the ethical guidelines expressed in the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice. Informed consent was obtained from all subjects.

## **Consent for publication:**

None, present study was retrospective study design and did not contains specific personal medical information (video or image) about an identifiable living individual.

## **Availability of data and materials:**

Yes, supplementary data. All data generated or analyzed during this study are included in this published article and its supplementary information files.

## **Competing interests:**

No.

## **Funding:**

This research was funded by the 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University (No. ZYGD20009).

## **Authors' contributions:**

Guarantor of the article: HT, HL. Study design: HT, HL, LYC. Drafting the manuscript: LYC, HL, HT. Statistical analyses and interpretation: CHL, HL. Data acquisition: LYC, CHL, SK, LYD, FHM, CML, LB, HL, HT. Critical revision of the manuscript: HT, LYC, CHL.

## **Acknowledgements:**

No.

## **Checklist for the appropriate reporting statement:**

STROBE (in supplementary file).

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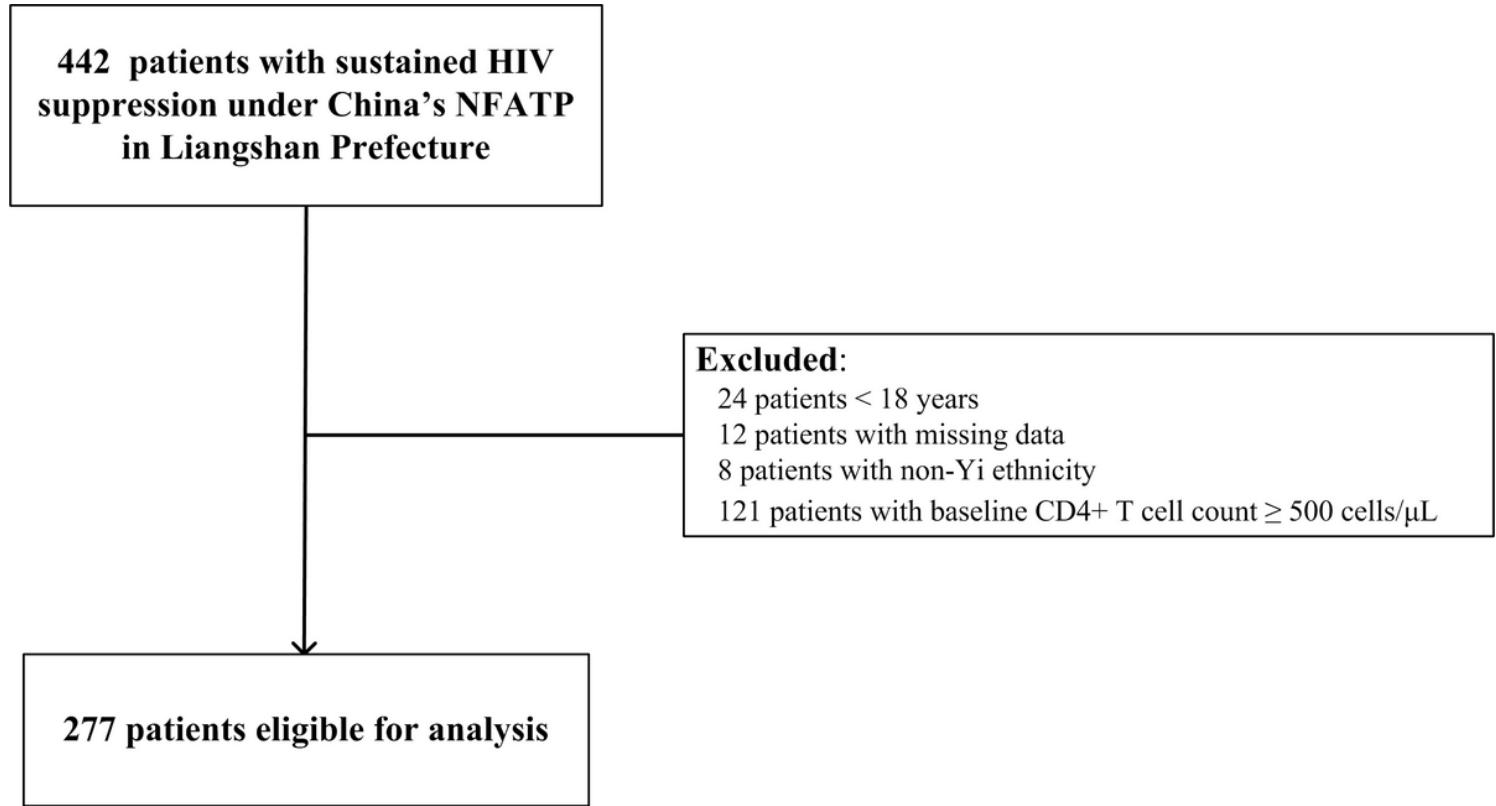
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## Figures



**Figure 1**

Map of Liangshan Yi Autonomous Prefecture in Sichuan province, southwest of China. All the HIV-infected Yi adults included in this study were from Zhaojue county (labelled red). Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.



**Figure 2**

Flow chart of this study.

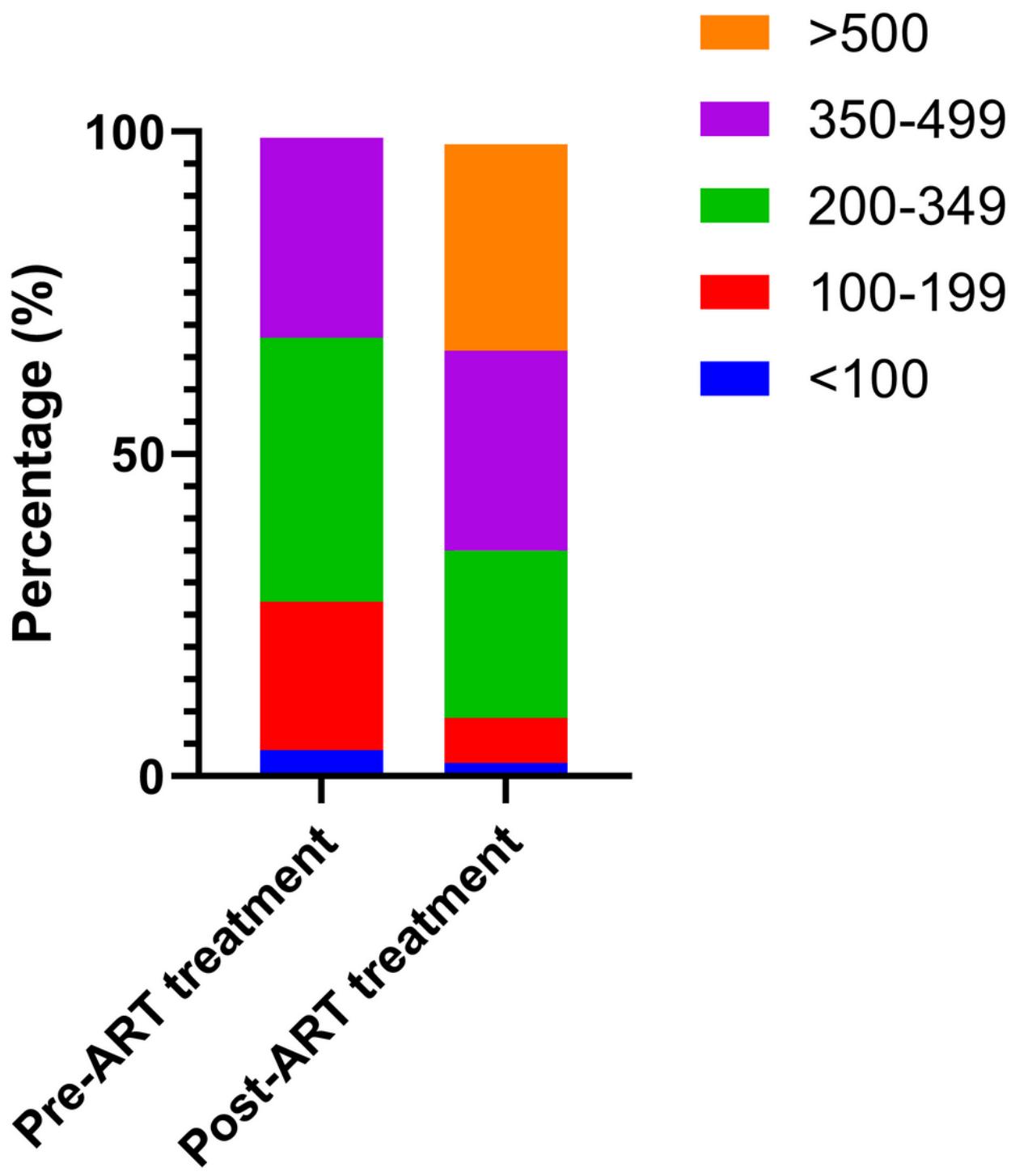


Figure 3

Proportion of Yi patients (n=277) stratified by CD4+ T cell count at baseline and the latest follow-up visit post-ART.

## Supplementary Files

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- [rawdata2021060802.xlsx](#)