Prevalence of HIV-1 Drug Resistance, Distribution of Subtypes and Drug resistance-associated mutations among Treatment-experienced Individuals in Chengdu, Southwest China, 2014-2016

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Research article

Keywords: HIV-1, Drug resistance, Subtypes, Drug resistance-associated mutations

Posted Date: October 21st, 2019

DOI: <https://doi.org/10.21203/rs.2.16258/v1>

Abstract

Background: The National Free Antiretroviral therapy (ART) Program in China has initiated to provide ART to HIV-1 patients, which may cause problems with drug resistance (DR). The number of HIV/AIDS patients in Chengdu ranks first in the national capital city. However, there is little data on the prevalence of HIV-1 DR in this region. Therefore, epidemiological surveillance was conducted on HIV-1 DR among patients receiving ART in Chengdu.

Methods: From 2014 to 2016, HIV/AIDS patients (15 years and older) who had received first-line ART for at least six months were enrolled in this study. Demographic, behavioral information and medical history were recorded, and blood samples were collected for viral loads and immune cell count analyses. HIV-1 pol was amplified, sequenced, and analyzed for HIV-1 subtypes and drug resistance-associated mutations (DRMs).

Results: A total of 13,782 individuals were enrolled and 653 cases were considered treatment failure after 6 months of ART. 481 (481/653) samples were amplified and sequenced successfully for subtypes and drug resistance analysis. Six subtypes were identified, among which CRF01_AE (54.3%) and CRF07_BC (41.6%) were the dominant subtypes, and CRF55_01B was detected in Chengdu for the first time. The overall prevalence of HIV-1 DR was 1.8%, with 1.2% to nucleoside reverse transcriptase inhibitors (NRTIs), 1.7% to non-NRTIs (NNRTIs) and 0.14% to protease inhibitors (PIs). The leading DRMs observed in the study were M184I/V (59.59%) against NRTIs and K103N (37.55%) against NNRTIs.

Conclusions: This study focused on the HIV-1 molecular surveillance among treatment-experienced individuals in Chengdu. The overall prevalence of DR was relatively low among treated patients. These findings were believed to be contributed to an understanding of HIV-1 subtypes, DR prevalence and DRMs profiles in Chengdu, and thereby optimizing clinical management, prevention and control of HIV.

Introduction

AIDS, also known as “acquired immunodeficiency syndrome”, is a highly malignant infectious disease caused by human immunodeficiency virus (HIV). It has been widely spread around the world, with approximately 36.9 million people living with HIV worldwide at the end of 2017 [1]. The situation of the HIV epidemic is a growing burden to public health in China. As of August 2018, it was reported that 841,478 people were living with HIV/AIDS in China, and the number of deaths was 259,200, ranking first among legal infectious diseases [2].

Application of highly active antiretroviral therapy (HAART) has significantly reduced the transmission of HIV and has decreased HIV-related morbidity and mortality [3–5]. In mid-2017, 20.9 million people infected with HIV were receiving antiretroviral therapy globally [1]. China has launched the National Free ART Program in 2002, which has acted as an efficient precaution for HIV. However, as accessibility of ART increases and improves survival rate, it may arouse concerns for drug resistance (DR) [6–9]. HIVDR poses a serious threat to the prevention of AIDS because it has the potential to affect the efficacy of the first-line

regimen. In addition, drug-resistant strains can be transmitted to newly infected individuals and are likely selected as dominant strains. HIVDR surveillance has made it possible to detect DR strains in time, evaluate and adjust treatment regimens, and reduce the transmission of DR strains.

Previous investigations of DR around the world have shown that the prevalence of DR varies from different regions, time period and target populations, and indicated that the overall incidence of treatment-naïve individuals is between 0% to 23% [10–12]. In the past decade, the proportion of DR in China has remained relatively low, at 3.8% in 2004 and 2005, and 3.6% in newly diagnosed HIV-infected people in 2015 [13, 14]. However, these reports are sporadic and limited and still require continuous monitoring to monitor changes in DR and adjust the first-line ART.

Sichuan is a representative province in southwest China and is adjacent to Yunnan and Tibet Autonomous Region. Chengdu is the capital city of Sichuan Province and acts as the political, economic, and cultural center of this area. In 1992, the first HIV–1 case in Chengdu was reported. National surveillance shows that HIV infection rates are incredibly high in Southwest China, and sex between men is clearly the main route of HIV transmission [15], especially in Chengdu, where HIV prevalence among MSM has remained high and the overall HIV prevalence was 15.5% from 2009 to 2014 [16], twice the national average (6.3%) [17].

By the end of 2016, a total of 18,603 people were living with HIV in Chengdu, which accounts for the largest HIV/AIDs population among other capital cities and 15,633 patients were receiving ART. However, there were little data on the prevalence of HIV–1 DR and drug resistance-associated mutations (DRMs) in this area. Therefore, epidemiological surveillance was conducted on HIV–1 subtypes, DR as well as DRMs profiles among patients receiving ART in Chengdu from 2014 to 2016,, and thus to optimize clinical management, prevention and control of HIV.

Methods

Study design, participants and specimen

This study was carried out at the Center for Disease Control and Prevention at Chengdu, Sichuan Province, West China. From 2014 to 2016, HIV/AIDS patients (15 years and older) who had received first-line ART for at least 6 months were enrolled in this study. The patients who carried resistance gene and were on second-line ART (<6 months) were excluded. Blood samples were collected in EDTA containers, and plasma was extracted and cryopreserved for analyses. Patients who provided written informed consent participated in the study. Demographic, behavioral information and medical history were recorded using a standard questionnaire.

Immune cells count and HIV–1 viral loads assay

To assess immune response, CD4⁺ T cells count was measured by flow cytometer BD FACSCount™ System (Becton Dickinson, Franklin Lakes, N. J., USA). HIV–1 RNA viral load (VL) was quantified with Abbott RealTime HIV–1 Amplification Reagent Kit (ABBOTT Molecular, Chicago, USA) and NUCLISENS EASYQ HIV–1 2.0 (BioMérieux, France) according to the manufacturer's instructions. VL more than 1000 copies/ml were considered as virologic failures and HIV–1 *pol* Gene were analyzed.

Amplification of HIV–1 *pol* gene

HIV viral RNA was extracted from plasma using Abbott RealTime HIV–1 Amplification Reagent Kit and then was synthesized into cDNA by using AccessQuick™ RT-PCR System (Promega, Madison, Wisconsin, USA). The *pol* gene fragments, containing the entire protease gene and partial reverse transcriptase gene (codons 1±300) were amplified by nested PCR (2×Pfu PCR MasterMix, Tiangen, Beijing, China). Primers and cycling conditions were previously described [18]. The DNA fragments were identified by 1.0% agarose gel electrophoresis. Then the products were purified and sequenced by Sangon Biotech Co., Ltd. (Shanghai, China).

Drug resistance-associated mutations analysis

The obtained nucleotide sequences were assembled, edited and aligned using ChromasProl.33 and Bioedit 7.0. HIV–1 subtyping was performed by constructing the HIV–1 *pol* phylogenetic tree (MEGA5.0). The sequences were then submitted to the Stanford HIV Drug Resistance Database (<http://hivdb.stanford.edu>) at Stanford University for the determination of DRMs. Drug resistance was divided into five levels: sensitive, potentially resistant, low resistant, moderate resistant and high resistant.

Statistical analysis

Statistical analysis was performed using SPSS Statistics version 22.0. Categorical variables were described in numbers and proportions. Possible associations of HIV–1 subtypes, HIV–1 drug resistance with demographic, exposure category and clinical variables were analyzed by using the Chi-square test or Fisher's exact test and logistic regression. All tests were two-sided with statistical significance at $p < 0.05$.

Results

Demographic characteristics of study participants and the prevalence of HIV–1 subtypes

Between 2014 and 2016, a total of 13,872 HIV-infected patients were tested for HIV–1 VL. 4.7% (653/13872) of cases, whose VL ≥ 1000 copies/ml were considered treatment failure. A total of 481 (481/653) samples were amplified and sequenced successfully for subtypes and genetic resistance.

Most of the subjects were male (411/481, 85.4%) and the main route of infection was heterosexual contact (342/481, 71.1%). The median age was 41 years (range: 15–81years), of which 50.3% were married. The demographic and subtypes distributions of 481 patients were presented in Table 1. Based on the generated sequences, six subtypes were identified. CRF01_AE (261/481, 54.3%) and CRF07_BC (200/481, 41.6%) were found to be the predominant subtypes. Other subtypes such as CRF08_BC (9/481, 1.9%), B (6/481, 1.2%), C (3/481, 0.6%) and CRF55_01B (2/481, 0.4%) were found in small proportions.

Prevalence and risk factors of drug resistance

According to the HIV DR Database, 245 DR cases were identified in 481 viral sequences. The overall prevalence of DR in 2014 to 2016 was 1.8% (245/13700, excluding sequencing failures). The comparison of characteristics between patients with and without HIV DR was listed in Table 2. Patients with HIV TDR were mostly male (85.3%, 209/245), and half of the patients were 25 to 45 years old (50.6%, 124/245), married (52.2%, 128/245) and contracted HIV via heterosexual route (71.8%, 176/245). Half of the cases have been treated for 1–3 years (52.2%, 128/245), most of whom received TDF + 3TC+ NVP/EFV regime and were infected with CRF01_AE (68.2%, 167/245).

Univariate analyses were conducted to correlate demographic characteristics with drug resistance. No differences were found between the prevalence of DR and gender, age at diagnosis, marriage status, infection routes, treatment duration, treatment change and VL (all $p>0.05$). CD4⁺ T cells count (≤ 200), CRF01_AE and “TDF + 3TC + EFV / NVP / other” are associated with DR ($p<0.00$). A logistic regression analysis showed there was no factor significantly associated with HIVDR.

Categories of antiretroviral drugs and susceptibility of drug resistance

In total, 1.2% of the samples were resistant to nucleoside reverse transcriptase inhibitors (NRTIs), 1.7% to non-NRTIs (NNRTIs) and 0.14% to protease inhibitors (PIs). The NRTI-associated mutations were forecasted to be highly resistant to Lamivudine (3TC, 67.8%, 146/245) and Abacavir (ABC, 40.4%, 99/245); resistant to Stavudine (D4T, 50.2%, 123/245), Tenofovir (TDF, 47.76%, 117/245); moderate- or low resistant to Azidothymidine (AZT, 7.3%, 18/245). 96.33% of the patients were predicted to have high resistance to Efavirenz (EFV) and Nevirapine (NVP), followed by resistance to Raltegravir (RPV, 67.0%, 169/245) and Etravirine (ETR, 67.3%, 165/245) (Figure 1). Twenty cases were identified to have drug resistance to PIs drugs, among which 15 cases belong to low or potential resistance.

The degree of drug resistance profiles

The prevalence of all DRMs to NRTIs, NNRTIs and PIs was displayed in Supplementary Table1. 14 DRMs were observed in NRTIs. The most commonly observed mutations with NRTIs were M184I/V(59.59%)

146/245), K65R (28.16% 69/245), D67N/G (19.18% 47/245), K70E/K/R (17.14% 42/245), Y115F (15.10% 37/245), L74I/V (11.02% 27/245) and T215I/Y (8.16%, 20/245). 16 DRMs were found in NNRTIs. K103N 37.55%, 92/245 was the most frequent mutation, followed by G190A/E/K/Q/S/V (28.57%, 70/245), V179I/D/E/T (27.76%, 68/245), V106A/I/M (26.12%, 64/245), Y181C/V (18.78%, 46/245), K101E/H/P (14.69%, 36/245), Y188C/H/L (5.71%, 14/245), L100I (4.08%, 10/245) and M230L (4.08%, 10/245). Three major PIs-associated DRMs and 7 secondaries were found in this study. The most frequent mutations were L10I/V (32) A71I/T/V (28) and K20I/R (26), among which L10I/V, A71I/T/V are nonsense mutations and K20I/R were predicted to have potential resistance to NFV.

The distribution of DRMs among different HIV–1 subtypes

14 NRTIs-associated DRMs were all found in CRF01_AE, and V75I/L/M, T69N/D and L210W were not found in CRF07_BC (Supplementary Table2). 16 and 15 (except A98G) NNRTIs-associated DRMs were found in CRF01_AE and CRF07_BC respectively. No significant difference was found in the distribution of NRTIs/NNRTIs-associated DRMs and CRF01_AE, CRF07_BC subtypes. NNRTIs-associated DRMs with extensively drug resistance such as G190A/E/K/Q/S/V, V179I/D/E/T, Y181C/V and K101E/H/P reside in CRF55_01B and subtype B, C. Only one case infected with CRF_08BC recombinant subtype showed TDR. E138A/G/R/K/Q was found in this case, and was predicted to have low/potential resistance to RPV and ETR. PIs-associated mutations only resided in CRF01_AE, CRF07_BC. The distribution of mutations in the PIs coding region was significantly different in the two recombinant subtypes ($P=0.05$). One patient infected with CRF07_BC recombinant subtype showed M46I, I47A and I50V 3 primary mutations, which was predicted to be resistant to all PIs.

Discussion

Since the 1980s, pioneers have focused on the issues of HIV DR [19]. With sustained efforts, technical protocols for HIV DR are becoming established. China has also compiled professional standards such as “Monitoring Strategies and Detection Techniques of HIV DR” to facilitate the comparison and utilization of various findings. 1793, 6005 and 6074 of HIV–1 infected patients undergoing ART were examined HIV–1 VL in Chengdu from 2014 to 2016. HIV–1 *pol* genes of 481 samples were sequenced in this study, and thus, HIV–1 subtypes, the prevalence of DR as well as profiles of DRMs were investigated.

Phylogenetic analysis identified four recombinant subtypes CRF01_AE, CRF07_BC, CRF08_BC, CRF55_01B and two subtypes B, C. Chengdu is an area with predominance of CRF01_AE and CRF08_BC, indicating a distinct subtypic heterogeneity compared to what has been shown in other regions [20, 21]. For instance, about half of the subtypes were identified as CRF08_BC (47.4%) among the recently infected population in Yunan [22] and CRF07_BC was the predominant strain in Xinjiang Province [23]. However, CRF01_AE were dominant in east China [24, 25]. It has been confirmed that one of the drug-trafficking routes in mainland China is from Yunnan to Sichuan and then to Xinjiang [26]. So it is assumed that subtypes in Chengdu is similar to Yunnan and Xinjiang provinces. In addition, novel CRFs

such as CRF55_01B were first discovered in Chengdu, and both cases were MSM. CRF55_01B was at first identified among MSM of China in 2013 and were subsequently reported in MSM in Shenzhen [27, 28]. These results specified the complexity of HIV subtypes in Chengdu and more interventions should be implemented.

The overall prevalence of DR studied subjects in 2014–2016 was 1.8% in Chengdu. The rate was relatively lower than that in other areas of China, such as Xinjiang, Yunnan and Jiangsu, and also lower than average rate of Sichuan [22, 23, 29, 30]. However, the rate varies a lot from previous reports in Chengdu, which reported that 17% (27/159) samples had DRMs among treatment-naïve HIV-infected individuals from 2007 to 2010 [31]. It can be attributed to different population, inclusion criteria and calculation methods. The prevalence of TDR indicates that the ART treatment in Chengdu is relatively efficient.

CD4⁺ T cells count, CRF01 AE and “TDF + 3TC + EFV / NVP / other” are associated with DR. Previous studies have suggested that patients with initial CD4⁺ T cells count > 200 cells/μl had better recovery of immune function after ART [32, 33]. The level of CD4⁺ T cells count may reflect the function of immune system, and the patients with poor immune function, that is primary CD4⁺ T cells count ≤ 200 cells/μl, are more likely to develop DR, indicating that HIV-infected patients should be detected early and initiate antiviral treatment as soon as possible.

The Chengdu ART regimen includes 3TC, one NRTI (AZT/D4T/TDF) and one NNRTI (EFV/NVP). The resistance to NRTIs was DDI (69.80%), 3TC (69.39%), FTC (69.39%), ABC (69.39%), D4T (50.20%), TDF (47.76%), AZT (13.47%) based on the number of the cases. Although FTC and DDI were not used in clinical settings, significant cross-resistance was observed. The structure, mechanism and efficacy of FTC are similar to 3TC, and FTC was predicted to have the same TDR profiles with 3TC. So is DDI with ABC. Under the 3TC-based medication regimen, a high proportion of drug resistance was observed in 3TC, most of which showed high and moderate resistance. Besides, the number of cases resistant to AZT is the lowest, most of which were low and have potential resistance. Thus, of 3TC+AZT is the best choice in the current NRTIs regimen, which is consistent with other reports [34].

In our study, M184I/V (59.59%) was the most prevalent mutation associated with NRTIs resistance in our study and was also frequently found in Europe, Africa and other regions in China [35, 36]. It alone causes high resistance to 3TC and FTC, low resistance to ABC and potential resistance to DDI. K 65R is one of the mutations with broad-spectrum resistance, and was found in more than one-quarter of the cases. Nine mutations associated with DR were observed in large proportions and resistant to many NNRTIs. K101 E / H / P, Y181 C / V, and G190 A / E / K / Q / S / V are broad spectrum general mutations resistant to all NNRTIs. The L100I and M230L mutations (4.08%) had low incidence and moderate or High resistance to RPV and ETR but no resistance to the first-line drugs EFV and NVP. These two mutations were found in CRF_01AE, CRF_07BC and subtype C, and patients with these two mutations were undergoing 3TC+TDF+EFV/NVP, indicating that this regimen may be related to these mutations. Three primary mutations M46I, I47A and I50V resistant to PIs were detected in one patient, whose regimen was

3TC+AZT+NVP then switched to LPV/r + 3TC+TDF. This patient showed decreased treatment adherence, and thus resulted in reduced effectiveness of treatment, indicating that clinicians should pay attention to compliance education to avoid similar cases and the transmitting of “super” resistant strains.

Patients infected with the CRF01_AE are associated with DR. All 14 NRTIs-associated mutations and 16 NNRTIs-associated mutations were all found in CRF01_AE. Both of the two cases identified with CRF55_01B both show DR, suggesting that this newly discovered CRF may likely develop DRMs. NRTIs-associated DRMs M184I/V and K65R and NNRTIs-associated DRMs with extensively drug resistance K101E/H/P, V179I/D/E/T, Y181C/V and G190A/E/K/Q/S/V were detected in CRF55_01B. PIs-associated mutations were found in 97 cases, most of which were secondary mutations like L10I/V, A71I/T/V and K20I/R, so, there were relatively few cases of DR. In this study, PI-associated DR mutations between CRF01_AE and CRF07_BC, K20I/R and T74S were mainly found in CRF01_AE while A71I/T/V, Q58E and V82I were frequently observed in CRF07_BC, indicates that different mutations may vary among different subtypes.

Conclusion

In this study, the HIV-1 genetic diversity and DRMs reveal various distributions among individuals receiving ART (>6 months) in Chengdu. The overall prevalence of DR remained low (1.8%) in the studied population. Surveillance of VL and DR in patients receiving ART is of great significance, which can track the evolutionary trends of different subtypes, adjust treatment regimens, and help to improve the quality of life. It also plays a considerable role to develop a clinical strategy and prevent the transmission of drug-resistant strains of HIV in this area.

Abbreviations

AIDS: Acquired Immune Deficiency Syndrome; HIV: Human Immunodeficiency Virus; WHO: World Health Organization; CRF: Circulating Recombinant Forms; VL: Virus load; NRTIs: Nucleoside reverse transcriptase inhibitors; NNRTIs: Non-nucleoside reverse transcriptase inhibitors; PIs: Protease Inhibitors; 3TC: Lamivudine; ABC: Abacavir; AZT: Zidovudine; D4T: Stavudine; TDF: Tenofovir; DDI: Didanosine; FTC: Emtricitabine; EFV: Efavirenz; NVP: Nevirapine; ETR: Etravirine; RPV: Rilpivirine; LPV/r: Lopinavir; ATV/r: Atazanavir; DRV/r: Darunavir; FPV/r: Fosamprenavir; IDV/r: Indinavir; NFV: Nelfinavir; SQV/r: Saquinavir; TPV/r: Tipranavir

Declarations

Competing interests

The authors report no conflict of interest connected with this study.

Funding

This study was supported by National Mega Projects of Science and Technology in 13th Five-Year Plan of China: Technical Platform for Communicable Disease Surveillance Project (2017ZX10103010–002).

Authors' contributions

PXF, CJY and LY designed the research; CJY, LY, LSJ, YD, SL, YL, GDH, GYS performed the research and acquired data; CJY, LY and YD analyzed the data; CJY, LY, LSJ and YD wrote the paper; PXF and BS revised the manuscript; PXF approved the final version to be published. All authors read and approved the final manuscript.

Acknowledgments

We are grateful to participants for their dedication and contribution to the research. We thank the support from the Public Health and Preventive Medicine Provincial Experiment Teaching Center at Sichuan University and the Food Safety Monitoring and Risk Assessment Key Laboratory of Sichuan Province.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Sichuan University, China. Written informed consent was obtained from the participants.

Availability of data and materials

All data generated or analyzed during this study are included in this article. All data and materials are presented in methods and results sections as shown in figures and tables. The datasets generated and/or analyzed during the current study are not publicly available due to policy of this project.

Consent for publication

Not applicable.

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Tables

Table 1. Demographic characteristics and HIV-1 subtypes of the study participants

	Participants	Subtypes					
		CRF01_AE	CRF07_BC	CRF08_BC	B	C	CRF55_01B
Total	481	261	200	9	6	3	2
Gender							
Male	411 (85.4)	222 (85.1)	175 (87.5)	4 (44.4)	5 (83.3)	3 (100.0)	2 (100.0)
Female	70 (14.6)	39 (14.9)	25 (12.5)	5 (55.6)	1 (16.7)	0 (0.0)	0 (0.0)
Age							
15~25	53 (11.0)	22 (8.2)	28 (14.0)	1 (11.1)	2 (33.3)	0 (0.0)	0 (0.0)
26~40	179 (37.2)	94 (36.0)	75 (37.5)	5 (55.6)	2 (33.3)	1 (33.3)	2 (100.0)
>40	249 (51.8)	145 (55.6)	97 (48.5)	3 (33.3)	2 (33.3)	2 (66.7)	0 (0.0)
Marital status							
Married/cohabiting	242 (50.3)	138 (52.9)	94 (38.8)	5 (55.6)	3 (50.0)	2 (66.7)	0 (0.0)
Unmarried	148 (30.8)	79 (30.3)	63 (42.6)	1 (11.1)	2 (33.3)	1 (33.3)	2 (100.0)
Divorced/widowed/separated	85 (17.7)	40 (15.3)	41 (48.2)	3 (33.3)	1 (16.7)	0 (0.0)	0 (0.0)
Unknown	6 (1.2)	4 (1.5)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infection routes							
Heterosexual contact	342 (71.1)	189 (72.4)	138 (69.0)	9 (100.0)	4 (66.7)	2 (66.7)	0 (0.0)
Homosexual contact	98 (20.4)	49 (18.8)	45 (22.5)	0 (0.0)	2 (33.3)	0 (0.0)	2 (100.0)
Blood transfusion	1 (0.2)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Intravenous drug injection	7 (1.6)	3 (1.1)	4 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	33 (6.9)	20 (7.7)	12 (6.0)	0 (0.0)	0 (0.0)	1 (33.3)	0 (0.0)

Table 2. Demographic characteristics of treatment-experienced HIV-1 individuals with virologic failure on ART and univariate analyses for correlates of drug resistance

Variables	Without DR	DR	<i>p</i> value
	n=236	n=245	
Gender			
Male	202 (85.6)	209 (85.3)	0.94
Female	34 (14.4)	36 (14.7)	
Age (Years)			
15~	24 (10.2)	21 (8.6)	0.84
25~	63 (26.7)	67 (27.3)	
35~	47 (19.9)	57 (23.3)	
45~	33 (14.0)	36 (14.7)	
≥55	69 (29.2)	64 (26.1)	
Marital status			
Married/cohabiting	114 (48.3)	128 (52.2)	0.70
Single	74 (31.4)	74 (30.2)	
Divorced/widowed/separated	44 (18.6)	41 (16.7)	
Unknown	4 (1.7)	2 (0.8)	
Infection routes			
Heterosexual contact	166 (70.3)	176 (71.8)	0.83
Homosexual contact	51 (21.6)	47 (19.2)	
IDU	4 (1.7)	3 (1.2)	
Unknown	15 (6.4)	19 (7.8)	
CD4+T cell count (cells/μl)			
≤200	78 (33.1)	177 (72.2)	0.00
≥200	151 (64.0)	65 (26.5)	
Unknown	7 (3.0)	3 (1.2)	
Treatment duration (year)			
0.5~	57 (24.2)	75 (30.6)	0.28
1~3	136 (57.6)	128 (52.2)	
≥3	43 (18.2)	42 (17.1)	
Treatment regimen			
AZT+3TC+EFV/NVP/others	91 (38.6)	64 (26.1)	0.00
D4T+3TC+EFV/NVP/others	26 (11.0)	24 (9.8)	
TDF+3TC+EFV/NVP/others	116 (49.2)	156 (63.7)	
3TC+EFV+NVP	3 (1.3)	0 (0.0)	
Unknown	0 (0.00)	1 (0.4)	
Treatment change			
Yes	8 (3.4)	17 (6.9)	0.07
No	228 (96.6)	228 (93.1)	
Viral load (log10)			
3~	130 (55.1)	111 (45.3)	0.10
4~	77 (32.6)	98 (40.0)	
≥3	29 (12.3)	36 (14.7)	
Subtypes			
CRF01_AE	94 (39.8)	167 (68.2)	0.00
CRF07_BC	131 (55.5)	69 (28.1)	

CRF08_BC	8 (3.4)	1 (0.4)
CRF55_01B	0 (0.0)	2 (0.8)
B	2 (0.8)	4 (1.6)
C	1 (0.4)	2 (0.8)

Figures

Figure 1

Drug types and their susceptibility of resistance level. Numbers of patients with TDR by NRTIs (A), NNRTIs (B) and their susceptibility of resistance level in Chengdu, 2014~2016. H: high resistance, M: moderate resistance, L/P: low or potential resistance

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