Analysis of factors associated with dropping-out from HIV antiretroviral therapy in Kunming City, China

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Abstract

Background: The implementation of national antiretroviral therapy (ART) and expanded ART policies results in that more and more HIV-infected patients receive ART in Kunming, Yunnan province, China. At the same time, however, the number of patients, who drop-out from ART, are also increasing. In this study, we explored the factors that may account for drop-out. Methods: Four hundred and thirty-nine HIV-infected patients, who received or used to receive ART, were recruited in this study. Their age is among 18 and 75. All patients were divided into two group: ART group (187 patients) and drop-out group (252 patients). Appropriate bio-statistics analysis, including univariate analysis and Multivariate analysis, were used to identify factors associated with drop-out. Results: Data from all patients were analyzed. Univariate analysis suggested that the factors associated with drop-out may include age, residential area, educational level, occupation, monthly income, the access to minimum living allowance, HIV transmission route, and living status. On the other hand, factors including area, monthly income, the access to minimum living allowance, and referral methods of follow-up institutions account for drop-out in multivariate analysis. Conclusions: This study identified a number of factors associated with drop out from ART. Based on our findings, appropriate interventions should be introduced decrease drop-out.

Background

Kunming is the capital city of Yunnan Province where located in the southwest of China. It has about 6.8 million population. The city is the political, economic and cultural center of Yunnan Province. In 1991, since the first local HIV-infected case was discovered, Kunming had became the one of the earliest provincial capital city that reported HIV infection in China. The AIDS epidemic in Kunming experienced the periods of introduction, rapid growth and effective containment. By the end of 2018, there are about 15,000 HIV-infected people survived from cumulative reported, accounting for 14% of the total surviving cases in Yunnan province. Antiretroviral therapy (ART) is the key and effective strategy for AIDS prevention and control. ART can prolong life for HIV-infected patients [1], and is also a major opportunity for HIV prevention since successful treatment of those already infected can prevent continued HIV transmission[2]. To improve treatment coverage rate, achieve
completely treatment success are the common goals of the country, health-care workers and HIV infected patients[3]. In 2015, UNAIDS is embarking on a fast-track strategy to end the AIDS epidemic by 2030[4]. Since the implementation of the national free anti-viral treatment and expanding treatment policies, the number of HIV infected people receiving ART is increasing[5,6], the number of people dropping out of ART is also increasing year by year[6,7]. Controlling the dropout rate of antiretroviral therapy can effectively reduce the mortality rate of AIDS, contribute to the implementation of the fast track strategy and to realize of the three 90% goals. This article analyzes the reasons and influencing factors of HIV-infected people dropping out of antiretroviral therapy in Kunming city, and explores the methods to reduce the rate of drop out.

Methods

Study setting, design, and population

The epidemic situation database and antiretroviral therapy database were derived from the National AIDS Integrated Prevention and Control Information System, deadline is August 31, 2018. HIV-infected people receiving antiretroviral therapy in the database were selected as the treatment group, those who had received antiretroviral therapy but are currently drop out as the drop out group. The types of drop out in this study includes drop out of follow-up and stop taking ART medicine.

HIV-infections from 14 counties of Kunming City were selected to participate in the survey. Kunming Center for Disease Control and Prevention were designed and conducted a questionnaire survey. Conducted a pre-investigation of qualitative interviews to control bias in the design stage of the project, then further revised and improved the questionnaire. After the questionnaire was formulated, the reliability of the questionnaire was assessed by retest method, and the consistency rate of the questionnaire was 0.86. Experts were asked to test the content and structure validity of questionnaire, experts believed the validity was good. According to the definition, inclusion and exclusion criteria to selected the subjects to control the selection bias. A questionnaire survey is conducted by trained investigators to make one-to-one interviews in order to control information bias. The contents of the questionnaire include demo graphical, services related to HIV treatment, etc.

In this study, strictly quality control was carried out in different stages of project design, data
collection and data analysis.

Definitions

Drop out of follow-up refers to after the appointed follow-up period more than 90 days, the patients do not actively contact the follow-up doctors or doctors could not contact the patient, and did not know the reasons for the discontinuation of treatment. Discontinuation refers to patients discontinuation of treatment for toxic side effects or various reasons, even doctors can contact patients, but patients no longer want to receive treatment[8].

Inclusion and exclusion criteria

Inclusion criteria for the drop out group were: (1) age 18-75; (2) those who dropped out of follow-up or stopped taking ART medicine after treatment; (3) those who cooperated with the investigators with informed consent; (4) those who without major diseases or mental disorders.

Exclusion criteria in the treatment group were: (1) age 18-75; (2) adherence to treatment after initiating antiretroviral therapy; (3) those who cooperated with the investigators with informed consent; (4) those who without major diseases or mental disorders.

Statistical analysis

When the questionnaire data were entered, verification documents were set to reduce the input errors. Double data entry consistency checks were carried out to detect and correct the input errors in time. Stata version 11.0 software was used for statistical data analysis. Univariate analysis was performed by Chi-square test, P value 0.05 was considered statistically significant. Meaningful factors in single-factor analysis were incorporated into multi-factor analysis. Logistic regression was used to analyze the influencing factors of the drop out of antiretroviral therapy. The level of significance was defined at P < 0.05.

Results

A total of 439 valid questionnaires were collected, of which 252 were in the drop out group and 187 were in the treatment group.
Social demographic characteristics and general situations of drop out group

There were 189 males and 63 females with mean age of 39.46±11.88 years. There were 215 cases of Han nationality (85.3%). The marital status was mainly unmarried or divorced, with 174 cases (69.0%). 176 (69.8%) of their educational level were junior high school or below. Their occupations were mainly farmers, housekeeping and unemployment accounting for 70.2% together. 84 cases (33.3%) had monthly income less than 500 yuan. 190 cases (75.4%) didn’t have minimum living allowances. In terms of transmission routes, 133 cases (52.8%) were heterosexual transmission, 43 cases (17.1%) were homosexual transmission, and 76 cases (30.1%) were intravenous drug use. 111 cases (44.0%) were living alone, 94 cases (37.3%) were living with their families.

Univariate Analysis of the General Situations

Univariate analysis was used to compare the treated group and drop out group according to age, gender, marital status, educational level, monthly income and other factors. The results showed that age, geographical division, educational level, occupation, monthly income, whether to receive the minimum living allowances, the route of infection, and living status had significant effects on the drop out of ART (P< 0.05).

Table 1. Comparison of general characteristics between treatment group and drop out group

| Item                | Treatment status during investigation | c2   |
|---------------------|--------------------------------------|------|
|                     | Drop out group (n=252) | treatment group (n=187) |      |
| Gender              |                        |                  |      |
| Male                | 18956.3                | 14743.8          | 0.78 |
| Female              | 6361.2                 | 4038.8           |      |
| Age                 |                        |                  |      |
| ≤24                 | 2461.5                 | 1538.5           | 11.37|
| 25-34               | 5847.5                 | 6452.5           |      |
| 35-44               | 9766.4                 | 4933.6           |      |
| 45-54               | 4758.0                 | 3442.0           |      |
| 55-64               | 1954.3                 | 1635.7           |      |
| ≥65                 | 743.8                  | 956.3            |      |
| Nationality         |                        |                  |      |
| Han nationality     | 21558.4                | 15341.6          | 0.97 |
| Ethnic minority     | 3752.1                 | 3447.9           |      |
| Region              |                        |                  |      |
| Countryside         | 14074.5                | 4825.5           | 39.16|
| Town                | 11244.6                | 13955.4          |      |
| Household register  |                        |                  |      |
| Local county        | 11958.6                | 8441.4           | 1.85 |
| Other county of the city | 2047.6        | 2252.4           |      |
| Other city of the province | 3959.1       | 2740.9           |      |
| Category                          | N     | %    |
|----------------------------------|-------|------|
| Other province                   | 7457.8| 5442.2|
| Marital status                   |       |      |
| Single                           | 8854.3| 5445.7|
| Married                          | 7160.2| 4739.8|
| Divorced                         | 8658.5| 6141.5|
| Bereaved wife or husband         | 758.3 | 541.7 |
| Educational level                |       |      |
| Illiteracy                       | 1090.9| 19.1  |
| Primary school                   | 5567.9| 2632.1|
| Middle school                    | 11166.5| 5633.5|
| High school                      | 3445.3| 4154.7|
| College or above                 | 4240.0| 6360.0|
| Occupation                       |       |      |
| Farmer                           | 11278.9| 3021.1|
| Housework and unemployment       | 6556.0| 5144.0|
| Service                          | 2739.7| 4160.3|
| Worker                           | 1137.9| 1862.1|
| Cadre staff                      | 733.3 | 1466.7|
| Retiree                          | 18.3  | 1191.7|
| Student                          | 1266.7| 633.3 |
| Migrant workers                  | 952.9 | 847.1 |
| Other                            | 850.0 | 850.0 |
| Monthly income                   |       |      |
| <500                             | 8475.0| 2825.0|
| 500-1000                         | 3666.7| 1833.3|
| 1000-2000                        | 3536.5| 6163.5|
| 2000-3000                        | 5054.3| 4245.7|
| ≥3000                            | 4755.3| 3844.7|
| Minimum living allowances        |       |      |
| Yes                              | 6278.5| 1721.5|
| No                               | 19052.8| 17047.2|
| Route of infection               |       |      |
| Injecting drug abuse             | 7683.5| 1516.5|
| Male to male transmission        | 4340.2| 6459.8|
| Heterosexual transmission        | 13355.2| 10844.8|
| Living status                    |       |      |
| Live alone                       | 11158.4| 7941.6|
| Usually live with strangers      | 2083.3| 416.7 |
| Live with classmates/colleagues/friends | 2765.9| 1434.1|
| Live with family                 | 9451.1| 9048.9|
| Recent CD4 counts                |       |      |
| <350                             | 12659.2%| 8740.8%|
| 350~                             | 4757.3%| 3542.7%|
| 500~                             | 79(54.9%)| 6545.1%|

Single factor analysis of antiretroviral therapy services

Through the single factor analysis of anti-virus treatment services provided by HIV/AIDS prevention and control institutions, it was found that referral methods provided by follow-up institutions and ART information provided by follow-up institutions were the influencing factors of dropping out of treatment (P < 0.05).

Table 2.A comparative analysis of ART for treatment group and drop out group
Multivariate logistic regression analysis

According to the above univariate analysis results, according to the inclusion criteria of \( P < 0.05 \), age, geographical division, education level, occupation, monthly income, whether to receive subsistence allowances, routes of infection, living status, referral methods provided by follow-up institutions and whether to provide ART information were taken as independent variables, and whether HIV-infected patients were dropped out or treated as dependent variables (drop out=0, treatment=1), with multivariate Logistic regression analysis. The results showed that HIV-infected patients living in rural areas were the risk factors for the drop out compared with those living in cities and towns. HIV-infected patients who has monthly income below 500 Yuan compared with 500-1000 yuan and 2000-3000 Yuan compared with more than 3000 Yuan monthly, not receiving minimum living allowances compared with who has minimum living allowances were the protective factors for drop out. Follow-up institutions offered referral methods in which carrying cards on their own was risk factors of drop out.

Table 3. Logistic regression analysis about the influencing factors of dropout

| Item                                                      | category | \( \beta \) | S.E  | \( Wald^2 \) | P     |
|-----------------------------------------------------------|----------|-------------|------|--------------|-------|
| First Result Notification institution                     | CDC      | 17961.5     | 11238.5 | 6.26         |       |
| Methadone maintenance sites                              |          | 350.0       | 350.0 | 350.0        |       |
| Antiviral treatment institution                          |          | 350.0       | 350.0 | 350.0        |       |
| Non-governmental Organizations                           |          | 847.1       | 952.9 | 350.0        |       |
| General Hospital                                         |          | 5250.5      | 5149.5| 350.0        |       |
| Other                                                     |          | 743.8       | 956.3 | 350.0        |       |
| Referral methods by follow-up institution                |          | 100.44      |       |              |       |
| Carry the card to go by oneself                          |          | 19677.8     | 5622.2|              |       |
| Doctors escort                                           |          | 5629.9      | 13170.1|             |       |
| ART information provided by follow-up institutions       |          | 14.33       |       |              |       |
| Yes                                                      |          | 22254.8     | 18345.2|             |       |
| No                                                       |          | 3088.2      | 411.8 |              |       |

Table 3. Logistic regression analysis about the influencing factors of dropout

| Item                  | category | \( \beta \) | S.E  | \( Wald^2 \) | P     |
|-----------------------|----------|-------------|------|--------------|-------|
| Age                   | ≤24      | -0.979      | 1.001| 0.957        | 0.328 |
|                       | 25-34    | 0.041       | 0.923| 0.002        | 0.964 |
|                       | 35-44    | 0.029       | 0.890| 0.001        | 0.974 |
|                       | 45-54    | -0.269      | 0.918| 0.086        | 0.769 |
|                       | 55-64    | -0.400      | 0.971| 0.170        | 0.681 |
|                       | ≥65      |             |      |              |       |
| Region          | Countryside | Town | 0.808 | 0.328 | 6.051 | 0.014 |
|-----------------|-------------|------|-------|-------|-------|-------|
| Education       | Illiteracy  | 0.282|       |       |       |       |
| Primary school  | -2.356      | 1.323| 3.197 | 0.074 |       |       |
| Middle school   | -0.852      | 0.587| 2.105 | 0.147 |       |       |
| High school     | -0.584      | 0.503| 1.347 | 0.246 |       |       |
| College or above| -0.091      | 0.478| 0.036 | 0.849 |       |       |
| Occupation      | Farmer      | 0.248|       |       |       |       |
| Housework and unemployment | -2.752 | 1.339| 4.227 | 0.040 |       |       |
| Service         | -2.022      | 1.327| 2.322 | 0.128 |       |       |
| Worker          | -1.699      | 1.340| 1.608 | 0.205 |       |       |
| Cadre staff     | -1.345      | 1.379| 0.951 | 0.330 |       |       |
| Retiree         | -2.220      | 1.413| 2.470 | 0.116 |       |       |
| Student         | -1.862      | 1.452| 1.645 | 0.200 |       |       |
| Migrant workers | -2.322      | 1.479| 2.464 | 0.117 |       |       |
| Other           | -2.005      | 1.433| 1.960 | 0.162 |       |       |
| Monthly income  |             |      |       |       |       |       |
| <500            |             |      |       |       |       | 0.016 |
| 500-1000        |             | 0.767| 0.505 | 2.307 | 0.129 |       |
| 1000-2000       |             | 0.522| 0.548 | 0.908 | 0.341 |       |
| 2000-3000       |             | 1.648| 0.509 | 10.490| 0.001 |       |
| ≥3000           |             | 0.478| 0.433 | 1.220 | 0.269 |       |
| Minimum living allowances |       |      |       |       |       |       |
| Yes             |             | -1.276| 0.404| 9.988 | 0.002 |       |
| No              |             |       |       |       |       |       |
| Route of infection | Injecting drug abuse |             |       |       |       |       |
| Male to male transmission | 2.317 | 1.196| 3.750 | 0.053 |       |       |
| Heterosexual transmission | 1.390 | 1.235| 1.266 | 0.261 |       |       |
| Living status   |             |       |       |       |       |       |
| Live alone      |             |       |       |       |       | 0.053 |
| Usually live with strangers | -0.665 | 0.304| 4.796 | 0.029 |       |       |
| Live with classmates/colleagues/friends | -1.449 | 0.749| 3.742 | 0.053 |       |       |
| Live with family | -0.820 | 0.499| 2.702 | 0.100 |       |       |
| Referral methods by follow-up institution | Carry the card to go by oneself |       |       |       |       |       |
Reasons for drop out of antiretroviral therapy in HIV-infected patients

The top three reasons for the drop out of antiretroviral therapy in HIV-infected patients were: serious side effects; need to persist in taking medicine regularly; Medication interruption due to imprisonment.

| Reason                                               | The number of response | The rate |
|------------------------------------------------------|------------------------|----------|
| Side effects are too serious to tolerate             | 87                     |          |
| to persist in taking medicine regularly is difficult | 72                     |          |
| Medication interruption due to imprisonment          | 67                     |          |
| Treatment information is asynchronous due to the change of current address | 60                     |          |
| No need to continue taking medicine for better health | 39                     |          |
| Consider that the treatment is ineffective           | 25                     |          |
| Family members do not support treating               | 14                     |          |

Discussion

Since China implemented the policy of four frees and one care, the drop out of ART has been an important issue affecting the therapeutic effect[9]. Drop out or not is an important index to measure the patient's treatment status and the success of treatment. Studies have shown that young, male, single or divorced[10], illiterate[11], the proportion of dropping out of treatment is higher. This study did not show that men were more likely to drop out. The higher the level of education is, the more difficult it is to drop out, which was consistent with the results of Mison Dahhab et al[12].

This study found that intravenous drug users were more prone to drop out, which was consistent with previous studies on the impact of injecting drug use on drop out[13]. Drug addicts are often managed by different institutions and departments, such as detoxification centers, prisons, methadone clinics, community antiretroviral therapy services institutions and so on. Job coherence among institutions should be strengthened to ensure that patients can receive sustained care and antiretroviral therapy in all institutions.
Multivariate analysis shows that regional division is the factor influencing the drop out of ART. The HIV patients who come from rural areas was more easily to drop out of ART than that in urban areas. On the one hand, because of the concentration of antiretroviral therapy institutions in cities or towns, the availability of antiretroviral drugs for HIV-infected patients in rural areas was not high due to long journeys or transportation costs. Foreign studies also showed that too long distance to get drugs in hospitals was one of the factors affecting the maintenance treatment of patients[14]. It is suggested that antiretroviral therapy points should be regulated scientifically, antiretroviral therapy points should be added within a reasonable distance, or ART drugs should be mailed to HIV infected patients to increase the availability of antiretroviral therapy services under the premise of strict confidentiality of personal privacy. On the other hand, others changed their mobile phone number of Kunming, which made the original treatment institutions unable to contact. Therefore, doctors should inform patients of referral information during treatment. In addition, they should leave as many contacts as possible that are not easy to replace such as QQ or WeChat, and the drug users should actively cooperate with doctors for treatment.

Multivariate analysis shows that the monthly income level and whether to receive a minimum living allowance are also important factors affecting the drop out of ART. It’s point out that reducing the cost of antiretroviral therapy for patients with financial difficulties deserves attention. Since the introduction of the ‘four frees and one care’ policy in 2003, our government has effectively provided more and more welfare policies for antiretroviral therapy, as well as free antiretroviral therapy. However, some of the inspection fees and transportation costs during antiretroviral therapy need to be paid by individuals. For the low-income HIV-infected patients, this may be the reason for the discontinuation of treatment. It is suggest that the cost of screening for HIV-infected patients with financial difficulties should be reduced appropriately.

This study includes a survey of antiretroviral therapy related medical services in the questionnaire. It is found that the mode of referral provided by follow-up agencies is an important factor affecting the drop out of antiretroviral therapy. Accompanied referral can greatly reduce the drop out rate of antiretroviral therapy, which is rarely mentioned in other studies. By establishing a
bridge between follow-up agencies and antiretroviral therapy points, the time from receiving their HIV diagnosis to timely treatment can be significantly shortened, the treatments of HIV-infected patients can be promoted, and the drop out of ART can be reduced[15]. It is suggested that further study should be conducted on the role of accompany referral in reducing the drop out rate.

This study found that HIV-infected patients believed that the main reason for the drop out was drug side effects. 34.5% of HIV-infected patients drop out of ART because drug side effects, which was consistent with the results of other domestic studies[16,17]. Therefore, health workers are required to carry out effective compliance education before antiretroviral therapy, increase the number of early follow-up visits. Once adverse drug reactions were found, psychological counseling should be given to the patients in time. And serious adverse drug reactions should be deal with in time, treatment plans should be adjusted as appropriate.

Limitations
Our study has some limitations. Firstly, due to the cross-sectional study with small sample size. And all the influencing factors are not included in the analysis, such as whether there are opportunistic infections before treatment, virological failure and other factors, which may cause bias. Therefore, it is necessary to track the drop out of treatment of HIV-infected patients in the future’s study.

Conclusion
This study indicated that we should strengthen the treatment and education for HIV-infected patients who is injecting drug use, low educational level or low economic level. Strengthen intervention measures, give financial supports and care assistance services. Strengthen AIDS-related medical services and government supports, so as to effectively improve the treatment retention rate and reduce the drop out rate of ART.

Declarations
Abbreviations

ART: Antiretroviral therapy; UNAIDS: United Nations Programme on HIV/AIDS; HIV: Human
immunodeficiency virus; AIDS: Acquired Immune Deficiency Syndrome; OR: Odds ratio; CI: Confidence interval

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Availability of data and materials
Data relating to this study are contained and presented in this document.

Authors’ contributions
BL and YL: Conceived and designed the study, reviewed literatures, extracted and analyzed data, interpreted results and drafted the manuscript. XWZ, Jun Liu, Jun Liang, WJH and BH: involved in study selection, data collection, extraction, quality assessment and reviewing the manuscript. JYW: analysis and interpretation, reviewed the manuscript thoroughly for its scientific content. All authors have read and approved the manuscript.

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Competing interests
The authors declare that they have no competing interests.
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