ORIGINAL RESEARCH

Adherence to antiretroviral therapy among HIV/AIDS patients in the context of early treatment initiation in Vietnam

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Purpose: This study aimed to assess the antiretroviral therapy (ART) compliance among patients with HIV/AIDS and its associated factors in the context of universal ART initiation in Vietnam.

Patients and methods: A cross-sectional survey was conducted in five ART clinics located in three provinces, such as Hanoi, Thanh Hoa, and Lao Cai, from July to September 2017. Overall, adherence to ART in the last month was measured using a 100-point Visual Analog Scale (VAS). Besides, information about forgetting doses in the last 4 days and delaying taking pills in the last 7 days was also reported.

Results: Among 482 patients, the suboptimal adherence rate was 54.5%. Noncurrent smoking (coefficient =4.19, 95% CI 0.42–7.97), higher baseline CD4 count (coefficient =4.35, 95% CI 0.58–8.13), and no traveling difficulties (coefficient =6.17, 95% CI 2.27–10.06) were predictors of higher VAS adherence score. Suboptimal adherence was associated with mountainous residence (OR =5.34, 95% CI 2.81–10.16). Female respondents were less likely to delay taking pills in the last 7 days (OR =0.19, 95% CI 0.07–0.52).

Conclusion: Our study embraced early ART initiation in Vietnam; however, this approach should be parallel with appropriate resource allocation and service delivery.

Keywords: HIV/AIDS, antiretroviral therapy, ART adherence, Visual Analog Scale, VAS

Introduction

HIV/AIDS has now evolved from an acute fatal disease to a chronic illness thanks to the extensive antiretroviral therapy (ART) access.[1] This treatment reduces mortalities, morbidities, and opportunistic infections and prolongs survival.[2,3] In addition, it helps to reduce HIV transmission in the community.[4,5] Therefore, enhancing ART coverage is a principle strategy to end HIV/AIDS. Until June 2017, there were more than 20.9 million HIV/AIDS individuals enrolling in ART program.[6] In 2015, the WHO promulgated a consolidated ART treatment guideline, promoting the universal ART access for all HIV-positive individuals regardless of CD4 cell count.[7]

Vietnam has adopted WHO's recommendations since 2017 with the decision number, 5418/QD-BYT, issued by the Ministry of Health.[8] These efforts have shown the strong commitment to the "90–90–90 goals" toward ending the AIDS epidemic by 2030.[9] However, this strategy is subjected to new challenges in the context of shrunken funds for HIV/AIDS control in Vietnam. Previously, approximately 95% of antiretroviral (ARV) drugs were funded by international organizations and only 5% from the government budget.[10] However, international funding resources have been speedily cut in recent years. Thus, early ART initiation may create greater financial

burdens among HIV patients. Moreover, being enrolled in ART at healthy stage possibly leads to disease optimism. A previous study suggested that "feeling healthy" is a strong predictor of ART refusal.[11] Although many studies in Vietnam have assessed the levels of ART adherence,[12,13] the potential mechanisms of how early ART eligibility may predict the levels of ART adherence have not been well studied. Therefore, our study aimed to assess the levels of ART adherence and associated factors among HIV/AIDS patients in the context of universal ART in Vietnam.

Patients and methods
Study settings
A cross-sectional study was conducted from July to September 2017 in three provinces: Ha Noi, Thanh Hoa, and Lao Cai. Hanoi represented an area with a diversity of HIV risk behaviors including unsafe sex practice and drug injection. Thanh Hoa represented a setting with the high prevalence of drug trafficking. Lao Cai is the embodiment of the mountainous area with the complexity of HIV risk behaviors as well as illicit drug trafficking due to a large border with other countries. Five chosen ART clinics included the following: Thanh Hoa Provincial HIV/AIDS Control Center, Quang Xuong General Hospital, Ung Hoa General Hospital, Ba Vi General Hospital, Bao Thang General Hospital. The first clinic was the provincial level, and the remaining clinics were the district level.

Study design and patient recruitment
We selected patients based on the following criteria: 1) being at least 18 years old, 2) being present during the study period, 3) having ARV treatment at chosen clinics, 4) agreeing to involve in the study, 5) not having cognitive disabilities. All the eligible patients were clearly explained about the study purposes. If they agreed to participate in the study, they were asked to provide a written informed consent to confirm their participation. There were 482 patients participating in the study.

Measures and instrument
A structured questionnaire was used for 20-minute face-to-face interviews. The collected information is given in the following sections.

Sociodemographic characteristics
Sociodemographic characteristics were as follows: age, location, marital status, education, employment, and travel difficulties.

Clinical characteristics
Data on Visual Analog Scale (VAS) adherence score, forgetting pills in the last 4 days, delaying taking pills in the last week were collected. We used 100-point VAS with 0 indicating "absolute non-adherence" and 100 indicating "excellent adherence" in the last 30 days.[14] VAS score equaling to at least 95% was defined as "optimal adherence"; otherwise, it was considered "suboptimal adherence."[15] Besides, the patients were asked whether they delayed taking pills in the last 7 days. Moreover, we asked patients to report HIV/AIDS stages, ART duration, and ART treatment satisfaction. Data on initial/last CD4 count were extracted from patients' medical records.

Risk behaviors
We collected information regarding current smoking, alcohol dependence, history of drug use/drug injection, and current drug use. Alcohol Use Disorders Identification Test-Consumption (AUDIT-C) was utilized to screen alcohol dependence with score ranging from 0 to 12. Patients were characterized as hazard drinkers if the score was 4 or above in males and 3 or above in females.[16] Current tobacco use was defined if patients smoked in the last 30 days.

Statistical analyses
Data were cleaned and analyzed by Stata (version 12; StataCorp LP, College Station, TX, USA). Missing data were handled using list-wise deletion strategy.[17] To identify differences between men and women, we utilized Mann–Whitney U, chi-squared, and Fisher's exact tests. Multivariate Tobit and logistic regression models were used to detect potential predictors of VAS adherence score, suboptimal adherence, and delayed taking pills in the last week. A stepwise backward model with P-value of <0.2 was used to reduce the regression models. Results were considered statistically significant if P-value was <0.05.

Ethical considerations
The study protocol was reviewed and approved by the institutional review board of Hanoi Medical University. Patients' personal information was completely confidential, and they could stop interviewing at any time or reject to answer any questions. For CD4 cell count, we also requested permissions from patients before extracting data from medical records.

Results

Table 1 summarizes the sociodemographic characteristics of respondents. The majority attained less than high school (66.0%), lived in urban areas (70.6%), and lived with spouse/partners (66.5%). Nearly 40% perceived barriers in traveling to ART clinics. The average age of males (39.3 years, SD =8.0) was higher than that of females (36.8 years, SD =8.4; $P<0.01$).

Most of the respondents had an initial CD4 cell count of ≥350 cells/mm^3 (53.0%), in which male respondents had higher baseline CD4 cell count than female respondents ($P<0.01$), which is summarized in Table 2. With regard to HIV stages, asymptomatic patients were dominant (82.6%) and only 3.9% were in AIDS stage. The average ART duration was 3.8 (SD =2.5), and approximately 93% were completely satisfied with ART treatment outcomes. The proportion of patients having methadone maintenance treatment (MMT) was 16.5%, in which the percentage of patients co-treated with MMT was higher in females than that in males ($P<0.01$).

The assessments of risk behaviors are summarized in Table 3. One-third of respondents were hazardous drinkers (38.5%), and more than half of patients reported that they were current smokers. Besides, 44.8% used to addict to the illicit drug, and 14.1% currently used the drug. The history of drug injection was commonly reported among respondents (41.2%). Rates of various health risk behaviors, such as hazard drinking, smoking, history of drug use/drug injection, and current drug use, were significantly higher among males in comparison with females ($P<0.01$).

Table 4 summarizes that the mean percentage of adherence in the last month was 89.3 (SD =8.2). There were 45.5% patients achieving optimal adherence, 3.9% patient forgetting taking pills in the last 4 days, and 12.5% delaying taking pills in the last week.

Table 5 summarizes that noncurrent smoking (coefficient =4.19, 95% CI 0.42–7.97), baseline CD4 count of at least 500 cells/mm^3 (coefficient =4.35, 95% CI 0.58–8.13), and no traveling difficulties (coefficient =6.17, 95% CI 2.27–10.06) were strong predictors of increased VAS score. Meanwhile, mountainous residence was associated with suboptimal adherence (OR =5.34, 95% CI 2.81–10.16). In addition, female respondents were less likely to delay taking pills in the last 7 days (OR =0.19, 95% CI 0.07–0.52).

Discussion

The current study endorses the high prevalence of ART suboptimal adherence among HIV/AIDS patients in the context of early ART eligibility in Vietnam. Mountainous residence, travel difficulties, and current smoking were strong predictors of suboptimal adherence. In contrast, being females and having initial CD4 counts of at least 500 cell/mm^3 were associated with optimal adherence.

The suboptimal adherence rate was considerably higher in comparison with previously published studies in Vietnam.[12,13] This may be due to the data collection time as we conducted this study after the implementation of early ART initiation program. Literature has highlighted that HIV individuals might be less motivated to comply with ART regimens when they are clinically asymptomatic.[11,18]

Table 1 Sociodemographic characteristics of respondents

Characteristics	Male		Female		Total		P-value
	n	%	n	%	n	%	
Education							0.60
Less than high school	194	65.5	121	66.9	315	66.0	
High school	89	30.1	49	27.1	138	28.9	
More than high school	13	4.4	11	6.1	24	5.3	
Geographic location							0.6
Rural	92	31.0	49	26.8	141	29.4	
Urban	84	28.3	58	31.7	142	29.6	
Mountainous	121	40.7	76	41.5	197	41.0	
Marital status							<0.01
Single	59	19.9	16	8.8	75	15.7	
Living with spouse/partner	218	73.7	100	55.0	318	66.5	
Divorced/separated/widowed	19	6.4	66	36.3	85	17.8	
Difficulty in traveling to the clinic							0.08
Yes	106	36.1	80	44.2	186	39.2	
No	188	64.0	101	55.8	289	60.8	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Age (years)	39.3	8.0	36.8	8.4	38.4	8.3	**<0.01**

Table 2 Clinical characteristics of respondents

Characteristics	Male		Female		Total		P-value
	n	%	n	%	n	%	
Initial CD4 count (cells/mm³)							<0.01
<200	77	33.1	21	16.3	98	27.1	
200–350	51	21.9	21	16.3	72	19.9	
≥350	105	45.1	87	67.4	192	53.0	
Last CD4 count (cells/mm³)							<0.01
<200	45	19.3	13	10.1	58	16.0	
200–350	55	23.6	15	11.6	70	19.3	
≥350	133	57.1	101	78.3	234	64.6	
HIV stage							0.30
Asymptomatic	156	74.6	105	79.6	261	76.5	
Symptomatic	53	25.4	27	20.5	80	23.5	
Co-treatment with MMT							<0.01
Yes	71	24.7	3	1.9	74	16.5	
No	217	75.4	158	98.1	375	83.5	
Treatment satisfaction							0.20
Totally satisfied	257	91.1	170	95.0	427	92.6	
Partially satisfied	24	8.5	8	4.5	32	6.9	
Not satisfied	1	0.4	1	0.6	2	0.4	
	Mean	SD	Mean	SD	Mean	SD	
ART duration	3.6	2.4	4.2	2.7	3.8	2.5	0.06

Abbreviations: ART, antiretroviral therapy; MMT, methadone maintenance treatment.

This hypothesis requires further studies to elaborate the potential mechanisms of how physical health status could predict ART compliance. Another potential justification was that early ART initiation could increase treatment costs for CD4/viral load tests and travels. A prior study in Vietnam indicated that the amount of willingness to pay for CD4/viral load testing was only a fraction of the current cost.[19] This highlights the importance of financial mobilization to ensure

Table 3 Health-related risk behaviors of respondents

Characteristics	Male		Female		Total		P-value
	n	%	n	%	n	%	
Hazard drinking							<0.01
Yes	172	57.9	12	6.6	184	38.5	
No	125	42.1	169	93.4	294	61.5	
Current smoking							<0.01
Yes	218	75.17	7	3.85	225	47.67	
No	72	24.83	175	96.15	247	52.33	
History of drug use							<0.01
Yes	208	70.0	7	3.8	215	44.8	
No	89	30.0	176	96.2	265	55.2	
Current drug use							0.68
Yes	140	68.6	4	57.1	144	68.3	
No	64	31.4	3	42.9	67	31.8	
History of drug injection							<0.01
Yes	191	64.8	6	3.3	197	41.2	
No	104	35.3	177	96.7	281	58.8	

Table 4 Self-reported adherence to ART

Characteristics	Male		Female		Total		P-value
	n	%	n	%	n	%	
Optimal adherence							<0.05
Yes	117	41.6	89	51.7	206	45.5	
No	164	58.4	83	48.3	247	54.5	
Forgot doses in the last 4 days							0.34
Yes	13	4.5	5	2.8	18	3.9	
No	274	95.5	175	97.2	449	96.2	
Delayed taking pills in the last week							<0.01
Yes	49	17.3	9	5.0	58	12.5	
No	234	82.7	171	95.0	405	87.5	
	Mean	SD	Mean	SD	Mean	SD	
VAS adherence score	88.8	12.8	90.2	15.6	89.3	8.2	<0.01

Abbreviations: ART, antiretroviral therapy; VAS, Visual Analog Scale.

the quality, adherence, and treatment outcomes, especially in the context of universal ART program in Vietnam.

The regression model showed that female patients were more likely to comply with treatment regimens. The result was in line with various studies in China,[20] sub-Saharan Africa, and Asia,[21] while contradictory results were affirmed in several studies in the USA,[22] British Columbia, and Canada.[23] The heterogeneity across studies, perhaps, could be explained by the sociocultural differences. In many Asian countries, husband–wife HIV transmission was highly prevalent due to the acceptance of husband's extramarital sex, delayed notification of husbands' HIV/AIDS status, and unawareness of husband's promiscuity.[24] Thus, we supposed that the passive HIV/AIDS infection motivated women to comply with ART regimens – the lifesaving. Besides, men have greater risks of diverse HIV risk behaviors such as multiple types of drug abuse,[25] alcohol use,[26] and tobacco use,[27] which were significant predictors of suboptimal adherence.[22,23,28,29]

Of note, mountainous residents were less likely to achieve optimal adherence. This issue may be due to socioeconomic disadvantages. A study by Tran et al in Vietnam revealed that ethnic minorities had lower access, adherence, and outcome of ART services due to socioeconomic inequity.[30] Besides, we observed a positive correlation between poor adherence and travel difficulty. We highly recommend the integration of ART in commune health centers to elevate the service accessibility. In fact, Vietnam successfully piloted the treatment 2.0 initiatives in 2011 regarding the joint initiative of WHO and the Joint United Nation Program on HIV/AIDS (UNAIDS). Five main elements included decentralizing and integrating HIV services into commune health centers; HIV testing, care,

Table 5 Factors associated with ART suboptimal adherence

Characteristics	VAS score		Suboptimal adherence		Delayed taking pills in the last week	
	Coefficient	95% CI	OR	95% CI	OR	95% CI
Sex (vs male)						
Female			0.63*	(0.36–1.09)	0.19**	(0.07–0.52)
Location (vs urban)						
Mountainous	−4.87***	(−9.00 to −0.74)	5.34**	(2.81–10.16)	0.44***	(0.19–1.00)
Employment (vs unemployed)						
Employed	−5.29***	(−9.62 to −0.96)	1.95***	(1.06–3.60)		
Education (vs <high school)						
High school	−2.84	(−6.79 to 1.12)				
>High school	8.02*	(−1.25 to 17.30)				
Travel obstacles (vs yes)						
No	6.17**	(2.27–10.06)	0.70	(0.41–1.19)	0.28**	0.14–0.58
Current smoking (vs yes)						
No	4.19***	(0.42–7.97)				
Initial CD4 count (vs <500 cell/mm^3)						
≥500 cell/mm^3	4.35***	(0.58–8.13)	0.35**	(0.17–0.72)		
Last CD4 count (vs <500 cell/mm^3)						
≥500 cell/mm^3			2.02*	(0.93–4.43)		

Notes: *$P<0.1$; **$P<0.01$; ***$P<0.05$.
Abbreviations: ART, antiretroviral therapy; VAS, Visual Analog Scale.

and treatment at the commune level; early diagnosis with quick tests; optimizing treatment regimens; and mobilizing community participation. Our findings embraced the expansion of this model in hard-to-reach locations.

It was noteworthy that those with high initial CD4 cell counts (>500 cell/mm^3) were more likely to achieve optimal adherence. We assumed that those with clinical symptoms might receive multiple drug regimens, leading to a higher likelihood of ART non-adherence due to pill burdens and drug interactions.[31] Some previous studies suggested that higher pre-ART CD4 cell count was associated with decreased mortality, improved treatment outcomes, and increased adherence.[32–34] Our findings supported the national guideline on HIV/AIDS care which increased the threshold of CD4 cell counts for ART initiation from <350 cell/mm^3 in 2011 to <500 cell/mm^3 in 2015, and most recently, enrolled all HIV-diagnosed patients in ART regardless of CD4 counts.

Our study affirmed smoking as a strong predictor of suboptimal adherence. It has been well evident that HIV-infected smokers are at greater risks of low CD4 counts, pulmonary infections, and lung cancer;[35] and nicotine dependence could alleviate health benefits of ART adherence.[36] While HIV-infected individuals are at greater risks of smoking than the general population,[37] tobacco cessation has been not properly paid attention in the HIV-infected group. Thus, it is called for pragmatic smoking cessation programs to minimize the

disease burdens and promote the treatment outcomes among HIV-infected patients.

The core implication of our study is that early ART initiation should be parallel with appropriate resource allocation and service delivery. This, perhaps, could be performed by mobilizing the government budget, including health insurance, and decentralizing/integrating HIV services into commune health centers. Besides, tobacco cessation programs should be implemented in ART clinics with dynamic forms such as behavioral therapies and nicotine replacement therapies.

Our study has several strengths. First, this current study provided up-to-date evidence on the level of ART adherence and associated factors in the context of early treatment in Vietnam. Thus, this current study would contribute to the benefits of early ART initiation. Second, as we recruited patients from urban, rural, and mountainous locations, it allowed us to obtain the sample size with diverse sociodemographic backgrounds, increasing the generalizability of the study population. Apart from these advantages, this study was subjected to several limitations. Although the self-reported measure was the most convenient method to evaluate ART adherence,[38] it might be subjected to recall and social desirability biases. Other direct methods such as therapeutic drug monitoring and biomarkers may promise more accurate results. Yet, costs and resources related to such methods should be taken into account. Besides, missing data might occur because patients could refuse to answer any questions

or provide any information. To minimize missing data, interviewers explained clearly about the study purposes and emphasized the assurance of information confidentiality.

Conclusion

Our study endorsed the high prevalence of ART suboptimal adherence among HIV-infected patients. Optimal adherence was associated with female patients or patients who had high baseline CD4 count, while suboptimal adherence was linked with mountainous residence and current smoking. While we embrace early ART eligibility in Vietnam, it should be parallel with improved resource allocation and service delivery.

Author contributions

HTM, BXT, GML, HTL, and HND conceived the study. BXT, CTN, GML, HTL, and HND designed the study. HTM, CTN, LTN, TPTT, and ATN implemented the study and collected the data. HTM, CTN, TPTT, LTN, and ATN analyzed the data. HTM, BXT, and GML drafted the first manuscript. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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