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Antiretroviral Therapy Adherence and Associated Factors Among Adolescents Living With HIV Aged 10-15 During the Covid-19 Pandemic: A Multicentre Cross-Sectional Study in Vietnam

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Abstract

Background

Adherence to antiretroviral therapy (ART) is essential for achieving viral suppression, preventing HIV-related complications, and improving long-term health outcomes. However, maintaining optimal adherence remains challenging among adolescents living with HIV (ALHIV).

Objectives

To evaluate the ART adherence and investigate the factors associated with ART non-adherence among ALHIV aged 10–15 years at five hospitals in Vietnam.

Methods

A cross-sectional study was conducted among 618 ALHIV aged 10–15 years receiving ART at five hospitals in Vietnam from May 2020 to October 2021. Data were collected through quarterly structured interviews and periodic medical record reviews. ART adherence was assessed using the average adherence across quarterly assessments. Non-adherence to ART was defined as an adherence level < 95%.

Results

Overall, 189 of 618 participants (30.6%) were classified as nonadherent. The most common reason for non-adherence was a lack of drugs at scheduled clinic visits (42.9%). ART adherence was significantly higher among those who initiated ART after 1–12 months of HIV diagnosis compared to within one month [AOR 0.58 (0.37–0.92)]. Virological treatment failure with viral load of 1.000-100.000 copies/mL at baseline was a risk factor for nonadherence [AOR 3.95 (1.30–11.9)] and those receiving HIV care at hospitals in Southern Vietnam [AOR 0.25 (0.15–0.44)]. Adolescents with married caregivers [AOR (0.57 (0.38–0.85)] had lower odds of nonadherence.

Conclusion

ART nonadherence remains common among adolescents living with HIV. Strengthening adherence preparation at ART initiation and providing ongoing support for caregivers may improve long-term treatment adherence and decrease virological treatment failure.

INTRODUCTION

Despite remarkable progress in expanding access to antiretroviral therapy (ART), adolescents remain one of the most vulnerable populations in the HIV epidemic. According to the United Nations International Children's Emergency Fund (UNICEF), while the number of new HIV infections has plateaued in recent years, the number of annual AIDS-related deaths occurring among children aged 0–14 years has declined by about 80 percent since its peak in 2002. In contrast, the number of annual AIDS-related deaths among those aged 15–19 has only decreased by 8 percent since 2002[1]. Globally, only 65% of adolescents living with HIV (ALHIV) aged 10–19 years were on antiretroviral treatment in 2023[2]. Since 2012, the number of HIV-related deaths has decreased with the expansion of

ART worldwide. Mortality among children living with HIV has decreased by 58% between 2010 and 2020; however, ALHIV mortality declined by only 36% in the same period[3]. In the era of antiretroviral therapy (ART), AIDS and opportunistic infections remain the second leading cause of death among adolescents globally[4].

Antiretroviral treatment is currently lifelong and improves immunocompetence, prevents HIV-related opportunistic infections, and saves resources[4,5]. ART with good adherence decreases the serum viral load to undetectable levels in people living with HIV[6] and decreases the risk for HIV transmission. Life expectancy is almost as high as that of the non-HIV population; hence, ART may be compared with insulin-dependent diabetes, a chronic disease that demands lifelong treatment. Adherence to ART plays an important role in achieving therapeutic efficacy. At least 95% of the prescribed ART is recommended for optimal adherence[7,8]. Nonadherence to ART leads to increased viral replication, virological treatment failure with a detectable viral load, selection of ART-resistant viral strains, immunological treatment failure, and finally clinical treatment failure with opportunistic infections and mortality[8–10]. ART resistance is an indication that ART should be changed to second- and third-line regimens, which are more expensive, increasing the burden of ART.

Adherence to ART among adolescents is challenging, as it is a complex health behaviour that is associated with many factors. Many studies have revealed that ART adherence among adolescents is lower than that among adults and young children[11–13]. Poor ART adherence may be related to psychosocial problems, patient-related factors, developing interest in romantic and sexual relationships where disclosure of HIV status may cause challenges, clinical and medication factors, and health system-based factors, including economic barriers to accessing HIV care [11,13]. Adolescence is a unique developmental period characterized by increasing autonomy, psychological vulnerability, and evolving relationships with caregivers. They often struggle with healthcare linkages and retention, with challenges during referral from paediatric to adult HIV outpatient care services[4]. They are expected to assume responsibility for medication-taking behaviours, while still depending on caregivers for emotional support, supervision, and healthcare engagement. They may lack adult support from their parents/caregivers, inadequate information, or may be misinformed about HIV and/or ART[14].

During the COVID-19 pandemic, lockdown restrictions have decreased HIV transmission but negatively affected the economic and psychosocial situation for ALHIV as well as access to healthcare services. As a result of lockdowns, limited accessibility to HIV services has challenged ART adherence. Globally, the low availability of ARV medicines due to inadequate human resources, raw materials, and other products in manufacturing and the limited and reduced income of people living with HIV due to COVID-19 has led to a loss of follow-up and affected the ART adherence[15]. A study conducted in Kenya[16] revealed that 17% of adolescents were concerned about running out of ART during the pandemic, and 5.1% reported skipping medication doses due to concerns about running out of ART medications[16]. Many studies conducted in Asia also showed the negative impacts of the COVID-19 pandemic on the ART retention and HIV care services[17,18]. In Vietnam, more than 30% of ALHIV reported a significant overall perceived impact of the COVID-19 pandemic[19].

According to data from Vietnam's Ministry of Health, over 200,000 people are living with HIV in Vietnam; of these, 2% are aged 0–14 years, and 3% are aged 14–19 years[20]. In Vietnam, evidence on ART adherence among younger adolescents aged 10–15 years remains limited. Existing studies have primarily focused on adults or older adolescents and were conducted before the COVID-19 pandemic. The pandemic introduced unprecedented disruptions to healthcare delivery and access to HIV services, potentially affecting treatment adherence among adolescents. How well did adolescents in Vietnam adhere to ART during the COVID-19 pandemic, and what variables

were linked to this adherence? This study aimed to determine the level of ART adherence and to examine factors associated with ART non-adherence among ALHIV aged 10–15 years at five hospitals in Vietnam.

METHODS

Study design and setting

This study was a cross-sectional study using data from the HIV-CHI II project. The HIV-CHI II cluster randomised controlled trial was implemented in five paediatric HIV outpatient clinics (OPCs) at the Vietnam National Children's Hospital (VNCH) in Hanoi, Hai Phong Hospital of Obstetrics and Paediatrics, Quang Ninh General Hospital, and the Children's Hospital (Nhi Dong) 1 and Children's Hospital (Nhi Dong) 2 (Ho Chi Minh City). The selection of these hospitals was based on the substantial number of HIV-infected adolescents receiving ART in their OPC's.

The study spanned a period of 12 months, encompassing both initial and quarterly investigations. However, due to the COVID-19 pandemic, data collection across the five hospitals could not be conducted according to plan. Consequently, the study timeline was extended by an additional 5 months beyond the originally planned duration. Therefore, the data collection spanned from May 2020 to October 2021.

Participants

Adolescents aged 10–15 years (as determined by their date of birth), diagnosed with HIV, and receiving treatment were included in this study. Participants were recruited from the five hospitals involved in the HIV-CHI II project. The decision to focus on the 10–15 age group was deliberate, as individuals aged 16–19 years were typically referred to adult OPCs in residential settings, making it challenging to engage with them for this study.

The adolescents included in the study were regularly checked up by doctors and received ART in one of the five hospitals following the guidance of the Ministry of Health. Nurses introduced patients and their caregivers to the project, invited them to participate, and obtained written consent for participation in the study. The exclusion criteria included patients from other settings who had temporarily received ART in the participating OPCs, as well as those residing in orphanages or other public facilities that may confound the project's intervention.

Sample size

We conducted a comprehensive sampling of all eligible patients across the five OPCs within designated hospitals. In May 2020, all 625 patients aged 10 to 15 who enrolled for ART at five OPCs were asked to participate in the study, along with their caregivers. Of the 625 patients, 618 fulfilled the inclusion criteria (including 189 in Vietnam National Children's Hospital, 59 in Hai Phong Hospital of Obstetrics and Paediatrics, 39 in Quang Ninh General Hospital, 186 in Children's Hospital 1, and 145 in Children's Hospital 2).

Data collection

Data collection involved two components: (1) conducting interviews with patients and their caregivers and (2) extraction of available information from outpatient medical records. The questionnaire was designed using Google Forms to facilitate electronic data entry through tablets and mobile phones. The questionnaire is found as a

supplementary file. Patients and caregivers were interviewed quarterly, and ART adherence was assessed in the week before interviewing at the beginning of the study, quarterly, and in the final survey.

Baseline data collection

At enrolment, outpatient clinic (OPC) nurses extracted the available information of participants from outpatient administrative medical records, including procedures, demographics, socioeconomic data of patients and caregivers, medical history, clinical status, and treatment progress. Baseline ART adherence (based on the 7-day recall), viral load, and CD4 count were also obtained at this time. All that information was filled in Google Forms on mobile phones.

Follow-up data collection

Data were extracted from routine quarterly clinic visits, which are part of standard HIV outpatient care in Vietnam. At each visit, nurses updated medical record information, including providing treatment progress, laboratory test results, and clinical outcomes. They conducted a brief structured interview with adolescents and their caregivers about medication-taking in the previous 7 days. The interviews yielded insights into medication administration, ART adherence, challenges, barriers, and recent problems.

During the final round of data extraction, an additional questionnaire was administered once to assess the impact of the COVID-19 pandemic on service access and socioeconomic hardship. Our research team developed a questionnaire drawing inspiration from the U.S Centers for Disease Control and Prevention report on the effects of COVID-19 on HIV patients, as well as the recent application of other survey tools to various population groups in the community. The questionnaire is found as a supplementary file.

Definition

Adherence is defined as patients taking ≥ 95% of the medication prescribed (< 2 doses of 30 doses or < 3 doses of 60 doses are missed), as documented by the ART healthcare provider. Non-adherence to ART is defined as patients taking < 95% [21,22].

In this study, ART adherence was assessed at the baseline and routine quarterly visits using a 7-day recall questionnaire administered to adolescents and caregivers. At each visit, adherence percentage was calculated based on the number of prescribed doses reportedly taken during the previous 7 days. For the purpose of this cross-sectional study, the average adherence across the four quarterly assessments was calculated for each participant.

Data analysis

For data analysis, the Stata version 17.0 (StataCorp LLC, College Station, Texas (TX), USA) was used. Numeric variables were summarized using means and standard deviations for approximately normally distributed data. Categorical variables were summarized as frequencies and percentages. Group differences were assessed using the Chi-square test or Fisher's exact test for categorical variables and the Student's t-test for continuous variables, depending on distributional assumptions.

Because participants were recruited from five hospitals, observations within the same study site may have been correlated, resulting in within-cluster correlation and potential heterogeneity across study sites. In this study, cluster-

robust variance estimation was not applied because of the limited number of study sites. Instead, the hospital site was included as a fixed-effect covariate in the multivariable logistic regression model to account for site-specific differences and reduce potential confounding due to variation across study locations.

The primary outcome was ART nonadherence, defined as having an average adherence level < 95%. Associations between each independent variable and the outcome were examined using bivariate analysis. Those variables found to have a *p* value of ≤ 0.2 were fitted to multivariable logistic regression. Odds ratios with 95% CIs were computed, and variables with *p* values ≤ 0.05 in the multiple logistic regression models were considered significantly associated with the dependent variable. For clarity of presentation, only variables with statistical significance or clinical relevance are shown in the main table.

Ethical issues

In accordance with Declaration of Helsinki, local regulations and guidelines ,the project received ethical approval from the Hanoi Medical University Institutional Review Board (Decision No HMUIRBI08/IBB-HDDDNCYSH-DHYHN, 29/04/2020). The ethical approval and consent given included approval to publish the study results. All potential ethical issues were discussed internally within the project team first and then, if needed, with the Hanoi Medical University Institutional Review Board. This is a sub-study of ClinicalTrials.gov ID NCT02035969 “Assessment of Group Peer Support to Children with HIV in Vietnam” Registration date 14/01/2014. Written consent to participate was obtained from the adolescent patients and their caregivers before participation in the study. The respondents could refuse or withdraw from the study at any time without any consequence. Adolescents were given a study identification number to ensure anonymity.

RESULTS

Sociodemographic characteristics

The study involved a total of 618 adolescents with HIV (referred to as patients) from OPCs in five hospitals in Vietnam (Table 1). The mean age (SD) of the patients was 12.8 (1.6) years. A greater percentage of males participated in the study, and the majority (91.9%) attended school. Approximately one-third of patients (29.3%) reported living in rented houses, and 3.9% were living with relatives. On average, the caregivers were 44.1 years old, 76.2% had an occupation, and 60.5% were married. More than half of the caregivers had a secondary/high school education (57.9%). Most caregivers reported experiencing fatigue, while more than 10% of caregivers were uncertain about their own fatigue status.

Table 1
Sociodemographic and household characteristics of the study participants and caregivers

I. Sociodemographic characteristics of patients		
Characteristic	**Total (N)**	**Frequency (%)**
Age (Mean, SD)	12.8 (1.6)	
Gender		
Female	299	48.4
Male	319	51.6
Poor family		
Yes	139	22.5
No	479	77.5
House ownership		
Own house	437	70.7
Rented house	181	29.3
Studying status		
No schooling	50	8.1
Go to school	568	91.9
Child's health insurance status		
Yes	613	99.2
No	5	0.8
Time duration to the clinic		
Less than 60 minutes	298	48.2
60–120 minutes	144	23.3
More than 120 minutes	176	28.5
II. Sociodemographic characteristics of caregivers		
Characteristic	**Total (N)**	**Frequency (%)**
Age (Mean, SD)	44.1 (11.3)	
Have an occupation		
Yes	471	76.2
No	147	23.8
Education level		
Primary school	175	28.3
Secondary and high school	358	57.9

I. Sociodemographic characteristics of patients		
Characteristic	**Total (N)**	**Frequency (%)**
Higher high school	85	13.8
Caregiver's HIV status		
No	197	31.9
Yes	399	64.6
Don't know	22	3.5
Caregiver's ARV treatment (n = 399)		
Yes	391	98.0
No	8	2.0
Marital status		
Not married	244	39.5
Married	374	60.5
Fatigue status		
Never	258	41.7
Sometimes	263	42.6
Often	14	2.3
Don't know	83	13.4

Table 1

Most of the patients (58.6%) started ART at the age between the ages of 1 and 5 years. Nearly half of the patients waited for 1–12 months before starting ARV treatment (44.3%). At baseline, most of the patients had been on ART for more than 10 years. Most of them were in clinical stage 1 (99.0%) and received a first-line ARV regimen (79.9%), with most ARV medication being an NNRTI-based regimen. Only a small number of patients (4.9%) changed their ART regimen during follow-up. The majority of patients were virologically suppressed below the detection threshold (86.4%) and had good immunocompetence, with a CD4 count over 500 cell/mm^3. (Table 2)

Table 2
Clinical and treatment characteristics of the study participants

Characteristic	Total (N)	Frequency (%)
Age of HIV diagnosis		
Below 1 year old	168	27.2
1–5 years old	362	58.6
Above 5 years old	88	14.2
Age of starting HIV treatment		
Below 1 year old	127	20.6
1–5 years old	353	57.1
Above 5 years old	138	22.3
Waiting time for ARV treatment		
1 month	200	32.4
From 1 to 12 months	274	44.3
Above 12 months	144	22.3
Years taking ART		
Below 5 years	43	7.0
5–9 years	190	30.7
Above 10 years	385	62.3
Baseline CD4 count (cell/mm3)		
Below 500	63	10.2
500–999	328	53.1
Over 1000	227	36.7
Baseline viral load (copies/ml)		
Below the detection threshold	534	86.4
< 1000	60	9.7
1.000-100.000	18	2.9
> 100.000	6	1.0
Baseline WHO stage		
Stage 1	612	99.0
Stage 2	6	1.0
Baseline ARV regimen		
First line	494	79.9

Characteristic	Total (N)	Frequency (%)
Second line	124	20.1
Number of daily ARV dose		
1 time	232	37.5
2 times	386	63.5
Baseline ARV medicines		
Boost PIs based	123	19.9
NNRTIs based	495	80.1
Change ARV regimen during follow-up		
No	588	95.1
Yes	30	4.9
Mental development		
Normal	608	98.4
Slow	10	1.6

Table 2

The status of adherence to antiretroviral therapy according to the WHO classification

A majority of the 618 patients in the study were routinely checked up (86.3%) according to the treatment guidelines. The reasons for the disruption of follow-up were the COVID-19 pandemic (69.4%), caregivers being busy (37.5%), and others (20.0%) (Table 3).

Table 3
Situation of monthly check-ups

Attributes	Total (N)	Frequency (%)
Routine follow-up status		
On time	533	86.3
Late 1–2 days	26	4.2
Late 3–7 days	56	9.1
Late above 7 days	3	0.4
Cause of routine follow-up late (n = 85)		
Due to COVID-19 pandemic	59	69.4
Due to caregiver busy	32	37.5
Others	17	20.0

Table 3

All patients (100%) indicated that they took the prescribed medication (Table 4), with the majority (91.6%) reporting no missed doses. Most patients (82.4%) adhered to a daily, on-time medication schedule.

Table 4
Patient daily medication adherence

Attributes	Total (N)	Frequency (%)
Taking the right ART dosage		
Yes	618	100
No	0	0
Monthly ARV missed doses		
No missed	566	91.6
Missed 1–2 doses	17	2.7
Missed 3–6 doses	16	2.6
Missed 7 doses and above	19	3.1
Monthly ARV late dose		
Not late	509	82.4
Late 1–2 doses	59	9.5
Late 3–6 doses	39	6.3
Late 7 doses and above	11	1.8

Table 4

One third of patients reported maintaining an adherence level of < 95% in the previous month (Table 5). The reasons for nonadherence to ART included a lack of drugs at the check-up (42.9%), late check-up (37.0%), and missed doses (20.6%).

Table 5
Adherence to antiretroviral therapy following WHO guidelines

Attributes	Total (N)	Frequency (%)
Level of adherence to ART		
Adherence	429	69.4
Nonadherence	189	30.6
Reason for nonadherence (n = 189)		
Monthly check-up late	70	37.0
Missed doses	39	20.6
Lack of drugs at the check-up	81	42.9

Table 5

Factors associated with nonadherence to antiretroviral therapy

In multivariable logistic regression analysis, adolescents who initiated ART within one month of HIV diagnosis had higher odds of ART nonadherence than those who initiated treatment after 1–12 months [AOR 0.58 (0.37–0.92)]. Higher odds of nonadherence were also observed among adolescents with a viral load of 1.000-100.000 copies/mL [AOR 3.95 (1.30–11.9)] and adolescents receiving HIV care at hospitals in Northern Vietnam [AOR 0.25 (0.15–0.44)]. Adolescents with married caregivers [AOR (0.57 (0.38–0.85)] had lower odds of non-adherence.

Table 6

Table 6
Factors associated with nonadherence to antiretroviral therapy

Variables		Adherence to ART		OR (95% CI)	AOR (95% CI)
		Adherence (n, %)	Nonadherence (n, %)		
Studying status	No attending to school	23	27	1	1
	Attending to school	406	162	0.34 (0.19–0.61)	0.77 (0.38–1.54)
Transportation time duration to outpatient clinic	Less than 60 minutes	197 (66.1)	101 (33.9)	1	1
	60–119 minutes	108 (75.0)	36 (25.0)	0.65 (0.52–1.02)	0.61 (0.37 - 1.02)
	More than 120 minutes	124 (70.5)	52 (29.5)	0.82 (0.55–1.22)	0.99 (0.62–1.57)
Hospital	Southern hospital	183 (55.3)	148 (44.7)	1	1
	Northern hospital	246 (85.7)	41 (14.3)	0.20 (0.14–0.31)	**0.25 (0.15–0.44)**
Caregiver's gender	Male	104 (63.8)	59 (36.2)	1	1
	Female	325 (71.4)	130 (28.6)	0.71 (0.48–1.03)	0.76 (0.48–1.19)
Caregiver's education level	Primary school	109 (62.3)	66 (37.7)	1	1
	Secondary and high school	252 (70.4)	106 (29.6)	0.69 (0.47–1.02)	0.98 (0.61–1.56)
	Higher than high school	68 (80.0)	17 (20.0)	0.41 (0.22–0.76)	0.96 (0.47–1.98)
Caregiver's occupation status	Have a formal occupation	324 (72.6)	129 (27.4)	1	1
	Have no occupation	87 (59.2)	60 (40.8)	1.83 (1.24–2.69)	1.19 (0.75–1.92)
Caregiver's marital status	Unmarried	155 (63.5)	89 (36.5)	1	1
	Married	274 (73.3)	100 (26.7)	0.64 (0.45–0.89)	**0.57 (0.38–0.85)**
Caregiver positive with HIV	No	126 (63.9)	71 (36.1)	1	1

**p-value < 0.05; CI: confidence interval; OR: odds ratio; AOR: adjusted odds ratio; ART: antiretroviral therapy.*

	Yes	287 (71.9)	112 (28.1)	0.69 (0.48–0.99)	0.94 (0.61–1.43)
	Don't know	16 (72.7)	6 (27.3)	0.67 (0.25–1.78)	0.96 (0.29–3.18)
Caregiver's fatigue status	Never	204 (79.1)	54 (20.9)	1	1
	Sometimes	170 (64.6)	93 (35.4)	**2.07 (1.39–3.06)**	1.05 (0.66–1.68)
	Often	9 (64.3)	5 (35.7)	2.09 (0.68–6.52)	0.86 (0.24–3.12)
	Don't know	46 (55.4)	37 (44.6)	**3.04 (1.79–5.14)**	1.12 (0.57–2.20)
Age of HIV positive confirmation	Below 1 year old	108 (64.3)	60 (35.7)	1	1
	1–5 years old	270 (74.6)	92 (25.4)	0.62 (0.41 0 0.91)	0.66 (0.29–1.48)
	Above 5 years old	51 (57.9)	37 (42.1)	1.31 (0.77–2.21)	0.89 (0.22–3.72)
Waiting time for ARV treatment	Less than 1 month	116 (58.0)	84 (42.0)	1	1
	From 1 to 12 months	201 (73.4)	73 (26.6)	0.50 (0.34–0.74)	**0.58 (0.37–0.92)**
	Above 12 months	112 (77.8)	32 (22.2)	0.39 (0.24–0.64)	0.53 (0.27–1.04)
Age of starting ARV	Below 1 year	81 (63.8)	46 (36.2)	1	1
	1–5 years	257 (72.8)	96 (27.2)	0.66 (0.43–1.01)	1.38 (0.57–3.35)
	Above 5 years	91 (65.9)	47 (34.1)	0.91 (0.55–1.51)	1.11 (0.27–4.50)
Level of CD4 cell at baseline	Less than 500 cell/ml	47 (74.6)	16 (25.4)	1	1
	500–999 cells/ml	235 (71.6)	93 (28.4)	1.16 (0.23–2.15)	0.92 (0.45–1.88)
	More than 1000 cells/ml	147 (64.8)	80 (35.2)	1.59 (0.85–2.99)	1.06 (0.49–2.27)

**p-value < 0.05; CI: confidence interval; OR: odds ratio; AOR: adjusted odds ratio; ART: antiretroviral therapy.*

The last viral load test until baseline	Below the detection threshold	373 (69.8)	161 (30.2)	1	1
	< 1000	43 (71.7)	17 (28.3)	0.92 (0.51–1.65)	1.14 (0.58–2.27)
	1.000-100.000	8 (44.4)	10 (55.6)	2.89 (1.12–7.47)	**3.95 (1.30–11.99)**
	> 100.000	5 (83.3)	1 (16.7)	0.46 (0.05–3.99)	0.42 (0.34–4.73)

**p-value < 0.05; CI: confidence interval; OR: odds ratio; AOR: adjusted odds ratio; ART: antiretroviral therapy.*

DISCUSSION

This multicenter study of 618 ALHIV aged 10–15 years found that 30.6% of adolescents were classified as nonadherent to ART, corresponding to an adherence rate of 69.4%. This adherence level was comparable to that reported in studies conducted in sub-Saharan Africa (65%)[13] and England (69%)[23], and slightly higher than the pooled global estimate of 62.3% among adolescent and young adults living with HIV[12].

However, our findings showed a lower adherence level compared to previous studies conducted in Ethiopia, Ghana, Brazil, and Vietnam. Specifically, in Ethiopia, 88.7% and 93.7% of children were adhering to ART at 7 and 3 days before an interview, respectively[11]. Similarly high adherence levels were reported in Ghana, with 93.2%[24], and in Brazil with 94%[25]. Several Vietnamese studies also indicated higher adherence levels, where patients were classified as adherent when receiving timely and sufficient ARV doses and checking up on schedule. These studies reported that the level of ART adherence was 91.1%[26], 78.9%[27], and 91.36%[28]. The lower adherence level observed in our study may be partly attributable to the fact that previous studies were conducted before the COVID-19 pandemic, whereas our study was undertaken during a period of substantial healthcare and social disruption.

The most common reason for nonadherence to ART in our study was a lack of ARV medication at the time of check-up (42.9%). Stockouts of medicine were still reported as a health service-related barrier to adherence to ART[29]. This problem became serious during the COVID-19 pandemic because of the pandemic's negative influence on access to healthcare services, as well as HIV care services globally. Physical distancing measures and lockdown, while effective in controlling the spread of COVID-19, led to reduced workforce availability in ARV manufacturing facilities and, subsequently, a lack of ARV medicines[15,30]. In this study, among nonadherent adolescents who lacked ARVs at follow-up, most of them (67/81 patients) came late to follow-up visits. Overall, 13.7% of adolescents in the study reported delays in attending follow-ups, with the primary reason being the COVID-19 pandemic. Decreased visits to hospitals/clinics and rescheduled appointments due to clinic closure during the COVID-19 pandemic were also reported by people living with HIV in a study conducted in 10 Asian countries, including Vietnam[17].

Although a longer travel time is often considered a barrier to HIV care[29] our findings suggest a more complex relationship. In the bivariate analysis, adolescents who traveled 60–119 minutes to the clinic had lower odds of ART non-adherence than those traveling less than 60 minutes. However, this association was no longer statistically significant after adjustment for hospital site in the multivariable model. This finding suggests that the observed

relationship between travel time and ART adherence may have been partly explained by differences across study hospitals rather than by travel time itself.

Indeed, adolescents receiving ART at the two hospitals in southern Vietnam had significantly higher odds of nonadherence than those receiving care at hospitals in northern Vietnam. A possible explanation is the unequal impact of the COVID-19 pandemic across regions during the study period. Southern Vietnam, particularly Ho Chi Minh City, experienced a more severe outbreak, resulting in prolonged lockdowns, disruptions to routine healthcare services, shortages of healthcare personnel, and increased pressure on hospital resources. The highest odds of reporting a significant overall perceived COVID-19 impact were also observed among ALHIV living in Ho Chi Minh City[19]. These challenges may have reduced access to outpatient HIV services and affected continuity of care among adolescents receiving ART. Although our study was not designed to directly evaluate hospital-level determinants, the findings highlight the potential influence of healthcare system disruptions on ART adherence during public health emergencies.

Many studies showed that the pandemic negatively impacted the HIV care services and HIV/AIDS-related services globally, as well as in many Asian countries[17,18]. For instance, in Myanmar, there was an interruption in ART retention and viral load testing because of the COVID-19 pandemic[18]. The study conducted in ten Asian countries also showed the interruption in ART or the decreased/complete stop of HIV prevention medication consumption[17]. These findings emphasise the significant impact of the COVID-19 pandemic on ART adherence, highlighting the need for robust strategies to mitigate such challenges during global health crises. In the context of social distancing restrictions, digital health interventions will play a crucial role in providing psychosocial support and ART adherence. A study conducted in Cameroon reported that two-way text messaging can increase attendance of paediatric patients at medical appointments for HIV care[31]. In the US, face-to-face visits were increasingly replaced by phone visits and video visits, with the highest proportion (50% of phone visits, and 30% of video visits) early in the COVID-19 pandemic; these proportions then decreased and plateaued for the remainder of the study period[32]. In Vietnam and several Asian countries, the use of telehealth services (phone consultation, video consultation, and remote refill of medications) remained limited among PLHIV[17]. However, about one-third expressed their preferences towards refilling of medications remotely or phone consultation with doctors/counsellors for future HIV telehealth services[17].

The COVID-19 pandemic highlighted the vulnerability of routine HIV care services to large-scale public health emergencies. To maintain ART retention during future pandemics or health crises, national HIV programs should develop emergent plans that ensure continuous access to ART. Lessons learned from the COVID-19 pandemic suggest that maintaining continuity of HIV care requires flexible service delivery models. Strengthening multi-month ART dispensing, expanding telemedicine, and improving coordination between HIV treatment facilities may help sustain treatment retention among adolescents living with HIV during future public health emergencies.

Additionally, ART adherence was assessed based on missed doses in the past month, whether the medication was taken at the correct time, and whether correct doses of medication were taken. This study revealed that all patients reported that they were taking the prescribed medication. The reported adherence in this study was higher than that of many other studies[12,13,21,23], however, lower than that reported in some Vietnamese studies, such as 99.6%[26] and 96.35%[28]. This finding demonstrated a high level of reported ART adherence among adolescents, which indicates that Vietnam has been successful in providing paediatric and adolescent HIV care services. The majority (87.7%) of patients reported taking the right number of ARV doses. However, in this study, the adherence rate to a daily, on-time medication schedule was 82.4%, which was lower than the findings of some studies, such as 98.34% [28] and 92.2% [26].

In this study, adherence to ART was significantly associated with the initiation of ARV treatment following HIV-positive confirmation. Patients who started treatment within the first month or had a duration of pre-ARV treatment preparation of less than 1 month demonstrated lower adherence to ART than did those who initiated treatment after 1 month of confirmation and beyond. A study in Nepal similarly identified nonadherence among patients who initiated ART within 24 months after diagnosis[33]. Delayed ARV treatment initiation was defined as starting treatment more than 30 days after diagnosis and was associated with poor HIV outcomes. Although the WHO recommended initiating ARV treatment as soon as possible after HIV diagnosis, patient education regarding the benefits of ART and the deployment of strategies to optimize care engagement and treatment adherence before the initiation of therapy are needed[8,34]. A lack of information about HIV or ART or the experience of ART side effects might increase the risk for nonadherence to treatment[35]. Pre-ART counselling and providing information on the ART regimen to patients and caregivers facilitates adherence[8]. Many authors have also noted an association between good adherence to ART and strong awareness of the benefits of ARV treatment[25]. Therefore, the keys to success in HIV treatment are education and adherence counselling.

Adolescents with baseline viral loads between 1,000 and 100,000 copies/mL had higher odds of ART non-adherence than those with viral suppression. Although unsuppressed viral load is more commonly regarded as a consequence of poor adherence[36,37], the relationship may be bidirectional. Adolescents with persistent detectable viral loads may experience treatment fatigue, psychological distress, and reduced confidence in treatment effectiveness. Previous studies have shown that psychological distress is associated with poorer medication adherence among adolescents living with HIV[38]. Furthermore, MacDonell et al. reported that greater motivational readiness was associated with optimal adherence and lower viral load[36]. Therefore, sustained virological non-suppression may be linked to reduced treatment self-efficacy and motivation to maintain adherence, which may manifest as missed doses, inconsistent medication-taking, or treatment interruption. However, given the cross-sectional design of this study, the temporal direction of the association between viral load and adherence cannot be established. Longitudinal studies are needed to better understand the direction of this association and to identify potential targets for interventions aimed at improving adherence among adolescents living with HIV.

Family and caregivers of patients play important roles in enhancing the level of adherence to ART among adolescents and children who remain dependent on adult supervision and assistance with medication administration[39]. Emotional symptoms were more common among caregivers of children living with HIV, as well as nonadherent children[40,41]. Previous studies showed that psychological distress, fatigue, and reduced treatment-related knowledge among caregivers may undermine effective support for paediatric ART adherence[42,43]. In the bivariate analysis, adolescents whose caregivers reported being uncertain about their fatigue status had higher odds of nonadherence. However, this association was no longer significant in the multivariable model. Although the adjusted analysis did not support an independent association between caregiver fatigue status and adolescent ART nonadherence, the finding may still suggest the importance of caregiver well-being and engagement in treatment support. Caregivers who are unable to recognize or report their own fatigue may experience emotional burden, reduced self-awareness, or difficulties in managing treatment-related responsibilities. Further research is needed to better understand how caregiver well-being influences ART adherence among adolescents living with HIV and to identify effective interventions to support both caregivers and adolescents.

With respect to the marital status of caregivers, those who were married were significantly nearly 40% less likely to be nonadherent to ART than those who were not married. A study in Ethiopia also showed the more optimal adherence to ART among children with married caregivers compared to those with a single caregiver[11]. Married

caregivers may benefit from shared responsibilities, emotional support from partners, and improved household organization, all of which can facilitate adherence to the complex ART regimen.

Despite widespread ART availability, a substantial proportion of adolescents remain at risk of suboptimal adherence. National HIV programs should prioritize adolescent-centered adherence strategies rather than relying solely on medication access. HIV care models should extend beyond the adolescent and formally recognize caregivers as a target population for support, education, and psychological interventions. Programs in low- and middle-income countries may benefit from integrated caregiver support into pediatric and adolescent HIV services to improve long-term treatment outcomes. Rapid ART initiation should be accompanied by adequate adherence preparation and caregiver counseling to ensure long-term treatment success. The findings contribute to the limited evidence based on ART adherence among adolescents in low- and middle-income countries and may inform the development of age-specific adherence support strategies.

Limitations of the study

Our study has several strengths and limitations. First, a major strength is the large sample size recruited from five hospitals during the COVID-19 pandemic, providing valuable real-world evidence on ART adherence among adolescents living with HIV in Vietnam under a major public health emergency. Second, the multicenter design enhanced the diversity of the study population. However, all participating sites were pediatric referral hospitals, which may limit the generalizability of the findings to adolescents receiving HIV care in district- or provincial-level health facilities.

Several limitations should also be considered. First, the cross-sectional study design precludes the establishment of causal relationships between the identified factors and ART non-adherence. Second, adherence was assessed based on reports from adolescents and their caregivers and may therefore be subject to recall and social desirability biases, potentially resulting in an overestimation of adherence.

Although the hospital site was included as a fixed-effect covariate in the multivariable model to account for site-specific differences, residual within-hospital correlation may still exist. Because clustering was not explicitly addressed in the estimation of standard errors, the precision of the reported confidence intervals may have been overestimated, potentially resulting in inflated statistical significance for some associations.

Finally, data collection was conducted over different periods across study sites due to disruptions caused by the COVID-19 pandemic. Because the severity of the pandemic, public health restrictions, and healthcare service availability varied over time, participants may have experienced different contextual factors affecting ART adherence. Although standardized procedures were implemented across all sites, temporal variations may have introduced residual confounding that could not be fully accounted for in the analysis.

CONCLUSION

ART non-adherence remains a substantial challenge among adolescents living with HIV in Vietnam. Early ART initiation after diagnosis, caregiver-related factors, virological status, and southern hospitals were associated with non-adherence. Strengthening adherence counseling and treatment preparation at ART initiation, providing support for caregivers, and ensuring continuous access to ART may help improve long-term treatment adherence in this population. Telemedicine should be expanded to ensure uninterrupted access to ART during future pandemics and other public health emergencies. Future studies are needed to better understand the relationships among

psychological distress, treatment perceptions, and ART adherence in both adolescents living with HIV and their caregivers.

Declarations

Ethics approval and consent to participate

In accordance with Declaration of Helsinki, local regulations and guidelines ,the project received ethical approval from the Hanoi Medical University Institutional Review Board (Decision No HMUIRBI08/IBB-HDDDNCYSH-DHYHN, 29/04/2020). The ethical approval and consent given included approval to publish the study results. All potential ethical issues were discussed internally within the project team first and then, if needed, with the Hanoi Medical University Institutional Review Board. This is a sub-study of ClinicalTrials.gov ID NCT02035969 “Assessment of Group Peer Support to Children with HIV in Vietnam” Registration date 14/01/2014. Written consent to participate was obtained from the adolescent patients and their caregivers before participation in the study. The respondents could refuse or withdraw from the study at any time without any consequence. Adolescents were given a study identification number to ensure anonymity.

Consent for publication

Not Applicable

Availability of data and materials

The data presented in this study are available upon request from the corresponding author. The data are not publicly available due to ethical application and approval.

Competing interests

None of the authors have any competing or conflicts of interest.

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Authors' contributions

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