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Characteristics of children with HIV/AIDS, adherence to antiretroviral treatment and related factors in a southern province of Vietnam.

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Abstract

Background: Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) remains a major concern in low and middle income countries, despite the enormous development of society today. Children with HIV/AIDS are the worst victim of the pandemic; adherence to Antiretroviral Treatment (ART) in children is inherently challenging.

Objectives: This study aimed to determine characteristics of children with HIV/AIDS, adherence to ART and related factors.

Methods: A cross-sectional descriptive study was collected on children diagnosed with HIV and receiving ART and their caregivers being managed at Soc Trang hospital for women and children, Soc Trang province, a Southern province of Vietnam.

Results: A total of 133 children were surveyed, mainly in the age of 11-15 years old (61.7%); females accounted for 57.1%; 87.2% of children suffered from malnutrition and clinical stage III accounted for mainly with the rate of 39.4%. Mostly children with advanced immunosuppression and severe immunosuppression accounted for 25.6% and 24.1%, respectively. The overall ART adherence rate in the study was slightly low at 26.3%. Factors associated with non-adherence to treatment include: Poor caregiver economics (p=0.028), caregiver education levels under grade 9/12 (p=0.049) and the patient's clinical stages were III and IV (p=0.042).

Conclusion: Most children with HIV/AIDS in Soc Trang, Vietnam were in advanced and severe condition, while ART adherence was greatly low. Factors associated with non-adherence include the caregiver's poverty, education and the child's clinical stage. Intervention programs should focus on addressing these objects to improve the adherence to ART.

Keywords: Children, HIV/AIDS, Adherence, Antiretroviral treatment, Related factors.

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Introduction

Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) remains a major concern in low-and middle-income countries, despite the enormous development of society today. According to WHO statistics in 2020, there were an estimated 37.7 million people living with HIV/AIDS worldwide, including 1.7 million HIV-infected children [1]. In Vietnam, within the first 6 months of 2017, the whole country detected 4,541 new cases of infection, 2,321 patients turned to AIDS, and 799 cases of AIDS died [2]. HIV/AIDS not only causes consequences for the economic, cultural and social development of each country, but also significantly affects the lives of those living with it. Children with HIV/AIDS are the worst victim of the pandemic; it can increase the incidence of infections and malnutrition in children. The number of cases currently under management in 2018 was 1.7 million children. The proportion of children infected with HIV compared to the total number of HIV infections worldwide was 4.5%. The estimated number of deaths from AIDS in 2018 was 100,000 children [2].

Antiretroviral drugs have been shown to be effective and safe to treat HIV/AIDS patients and Antiretroviral Treatment (ART) is increasingly being expanded in many countries, especially low-and middle-income countries [3,4]. However, adherence to treatment in children is inherently challenging because most children have to rely on caregivers instead of self-medication or follow-up visits. When children with HIV do not adhere to ART, it not only affects their own quality of life but also increases the risk of HIV transmission to others. Many studies have suggested that, suboptimal adherence has both clinical and economic consequences, including accelerated disease progression and mortality, decreased health-related quality of life, and higher healthcare costs [5].

Soc Trang, an economically disadvantaged province in the south of Vietnam, where scientific research on children with HIV/AIDS has not received much attention. Up to now, there have been no studies on the characteristics of children with HIV/ADIS; adherence to ART and related factors. This study was conducted to find out the cause of non-adherence to treatment so that appropriate remedial measures could be taken.

Materials and Methods

Ethics statement

This study was approved by the ethics committee in biomedical research of Can Tho university of medicine and pharmacy, Can Tho City, Vietnam (No. 107/HĐĐĐ-PCT). The purpose of the research is to serve science and people, towards the benefit of the community on the treatment of HIV/AIDS in children.

Study design

A cross-sectional descriptive study was collected on children with HIV/AIDS to determine demographic, clinical characteristics and immune status of patients; adherence to ART and related factors.

Subjects and study setting

The subjects in this study were children diagnosed with HIV and receiving ART and their caregivers being managed at Soc Trang hospital for women and children, Soc Trang province, Vietnam from June 2020 to June 2021.

Selection criteria:

- Children were diagnosed with HIV according to WHO criteria [6].
- HIV virological assay: For children ≤ 18 months old.
- HIV serological assay: For children over 18 months old to ≤ 15 years old.
- Children were receiving ART.

Exclusion criteria: Caregivers do not consent to children participating in the study.

Sample size: A total of 133 children with HIV/AIDS were examined and treated as outpatients at Soc Trang hospital for women and children and their primary caregivers.

Sampling method: Convenience sampling.

Measurements and Data Collection

All children were collected the followings:

Epidemiological, clinical characteristics and immune status

- **Demographic characteristics of children:** Age, gender, ethnicity, geography.
- **Caregivers characteristics:** Economy, primary caregivers, education level.

Clinical characteristics of children

- **Malnutrition:** Based on weight/height, determined according to WHO standards [7].
- **WHO clinical staging of children with HIV/AIDS:** *(1) Stage I when the child had asymptomatic, persistent generalised lymphadenopathy; (2) Stage II when the child had hepatosplenomegaly, papular pruritic eruptions, recurrent oral ulcerations, parotid gland enlargement, herpes zoster, recurrent respiratory tract infections; (3) Stage III when the child suffered from unexplained moderate malnutrition, persistent diarrhea/fever, oral candidiasis, pulmonary tuberculosis, severe recurrent presumed bacterial pneumonia, acute necrotizing ulcerative gingivitis or stomatitis or acute necrotizing ulcerative periodontitis, unexplained anaemia (<8 g/dl) and or neutropenia (<500/mm3) and or thrombocytopenia (<50,000/mm^3) for longer than one month; (4) Stage IV when the child had nexplained severe wasting or severe malnutrition not adequately responding to standard therapy, recurrent severe presumed bacterial infection, chronic herpes simplex virus infection, extra pulmonary tuberculosis, HIV encephalopathy, HIV-associated nephropathy, HIV-associated cardiomyopathy [8].*
- **Immune status of children:** Based on CD4 cell count by age, according to WHO criteria, classified into 4 levels; not significant immunosuppression, mild immunosuppression, advanced immunosuppression and severe immunosuppression (Appendix) [8].

Immune status	Age		
	Up to 12 months	13-59 months	5 years or over
Not significant immunosuppression	>35%	>25%	>500/mm3
Mild immunosuppression	25%−34%	20%−24%	350−499/mm3
Advanced immunosuppression	20%−24%	15%−19%	200−349/mm3
Severe immunosuppression	<20%	<15%	<200/mm3

Appendix. CD4 levels in relation to the severity of immunosuppression [8].

Adherence to treatment

Adherence to ART in children was assessed according to the guidelines of the ministry of health of Vietnam [9], based on the followings: 1) Patient had first CD4 test within 15 days of treatment registration; 2) Patients eligible for ART were started on ART within 15 days; 3) Routine HIV load testing every 6 months for patients on ART <12 months and every 12 months for those on ART ≥ 12 months; 4) Patients were tested for CD4 at least every 6 months after treatment registration; 5) Patients were monitored for weight and height at all follow-up visits within the last 3 months; 6) Patients were monitored for clinical stage at all follow-up visits within the last 3 months; 7) Patients were monitored for adverse effects of the drug at all follow-up visits within the last 3 months; 8) Patients had an opportunistic infection at all visits within the last 3 months; 9) Patients were monitored for clinical symptoms of tuberculosis at all follow-up visits within the last 3 months; 10) Patients had a routine follow-up visit at least once within the last 3 months; 11) Patients were on time for all appointments within the last 3 months; 12) Caregivers gave children enough medicine, not forgetting the dose. Overall treatment adherence was determined when achieving factors 10) and 11) and 12) and 75% of factors from 1) to 9).

Statistical Analysis

Data analysis and processing methods

SPSS 20.0 software Calculate frequencies and percentages for qualitative variables. Compare the difference between the two ratios based on the chi square test and $p<0.05$ recorded a statistically significant difference.

Results

Epidemiological, clinical characteristics and immune status in children with HIV/AIDS

A total of 133 children were invited to participate in the study, mainly in the age group of 11-15 years old (61.7%), then 2-10 years old (34.6%). Females were slightly higher than males with the rate of 57.1% and 42.9% respectively. Kinh ethnic group accounted for the majority with the rate of 70.7%, the Khmer ethnic group accounted for 28.6%. The percentage of children residing in urban areas was 32.3%; rural areas accounted for 67.7% (Table 1).

Epidemiological characteristics		Frequency (n=133)	Rate (%)
Age	<2 years old	5	3.8
	2-10 years old	46	34.6
	11-15 years old	82	61.7
Gender	Male	57	42.9
	Female	76	57.1
Ethnicity	Kinh	94	70.7
	Khmer	38	28.6
	Chinese	1	0.8
Geography	Urban areas	43	32.3
	Rural areas	90	67.7

Table 1. Epidemiological characteristics of children with HIV/AIDS.

The majority of caregivers for children with HIV/AIDS were economically poor, accounting for 63.9%. The primary caregivers were mainly parents (81.2%), followed by grandparents (11.3%); 67.7% had an education level < grade 9/12 (Table 2).

Characteristics of caregivers for children		Frequency (n=133)	Rate (%)
Economy	Poor	85	63.9
	Medium	40	30.1
	Pretty rich	8	6
Primary caregivers	Parents	108	81.2
	Siblings	1	0.8

	Grandparents	15	11.3
	Others	9	6.8
Education level	≤ grade 9/12	90	67.7
	> grade 9/12	43	32.3

Table 2. Characteristics of caregivers for children.

Among children with HIV/AIDS, 87.2% of children suffered from malnutrition; clinical stage III accounted for mainly with the rate of 39.4%; 47.2% of children with recurrent respiratory infections; 44.1% popular pruritic eruptions; 19.5% persistent fever; 17.3% oral candidiasis, 15.7% persistent diarrhea. In terms of immune status, mostly children with advanced immunosuppression and severe immunosuppression accounted for 25.6% and 24.1%, respectively (Table 3).

Clinical characteristics and immune status		**Frequency (n=133)**	**Rate (%)**
Malnutrition		116	87.2
Localized or systemic lymphadenopathy		7	5.3
Clinical stage	Stage I	23	18.1
	Stage II	33	26
	Stage III	50	39.4
	Stage IV	21	16.5
Papular pruritic eruptions		59	44.4
Recurrent respiratory tract infections		62	46.6
Persistent fever		26	19.5
Oral candidiasis		23	17.3
Pulmonary tuberculosis		4	3
Extrapulmonary tuberculosis		3	2.3
Severe septic		3	2.3
Persistent diarrhea		20	15
Anemia		52	39.1
Immune status	No significant immunosuppression	21	15.8
	Mild immunosuppression	30	22.6
	Advanced immunosuppression	34	25.6
	Severe immunosuppression	32	24.1
	Not tested	16	12

Table 3. Clinical characteristics and immune status of children infected with HIV/AIDS.

Adherence to treatment of children with HIV/AIDS

The treatment monitoring tests were not well performed according to the protocol: Only 47.4% of children had the first CD4 test within 15 days of being diagnosed with HIV; 69.9% of children were performed for CD4 count test and 72.2% for HIV load test periodically. Issues that were much better taken care of were side effects monitoring (100%) and opportunistic infections monitoring (100%); clinical symptoms of tuberculosis monitoring (99.2%); clinical stage follow-up (97.7%); weight and height monitoring (95.5%). Up to 94.0% of children had periodic follow-up visits, 69.9% of children had follow-up visits on time and 44.4% of children adhered to correct medication. In summary, the overall ART adherence rate in the study was slightly low at 26.3% (Table 4).

Characteristics of children with HIV/AIDS, adherence to antiretroviral treatment and related factors in a southern province of Vietnam.

Treatment adherence	n	%
Patient had first CD4 5 days of treatment registration	63	47.4
Patients eligible for ART were started on ART within 15 days	109	82
Routine HIV load testing every 6 months for patients on ART <12 months and every 12 months for those on ART ≥ 12 months	96	72.2
Patients were tested for CD4 at least every 6 months after treatment registration	93	69.9
Patients were monitored for weight and height at all follow-up visits within the last 3 months	127	95.5
Patients were monitored for clinical stage at all follow-up visits within the last 3 months	130	97.7
Patients were monitored for adverse effects of the drug at all follow-up visits within the last 3 months	133	100
Patients had an opportunistic infection at all visits within the last 3 months	133	100
Patients were monitored for clinical symptoms of tuberculosis at all follow-up visits within the last 3 months	132	99.2
Patients had a routine follow-up visit at least once within the last 3 months	125	94
Patients were on time for all appointments within the last 3 months	93	69.9
Caregivers gave children enough medicine, not forgetting the dose.	59	44.4
Overall treatment adherence	35	26.3

Table 4. *Status of treatment adherence.*

Factors associated with non-adherence to treatment include: poor caregiver economics (p=0.028), caregiver education level ≤ grade 9/12 (p=0.049) and the patient's clinical stages were stages III and IV (p=0.042). Factors such as age, gender, ethnicity, geography, primary caregiver, infectious diseases, side effects and immune status were not related to ART adherence (Table 5).

Related factors		Non-adherence n(%) (n=98)	Adherence n(%) (n=35)	p-value
Age	≤ 10 years old	37 (72.5)	14 (27.5)	0.815
	11-15 years old	61 (74.4)	21 (25.6)	
Gender	Female	44 (77.2)	13 (22.8)	0.426
	Male	54 (71.1)	22 (28.9)	
Ethnicity	Kinh	66 (70.2)	28 (29.8)	0.158
	Others	32 (82.1)	7 (17.9)	
Geography	City	29 (67.4)	14 (32.6)	0.258
	Countryside	69 (76.7)	21 (23.3)	
Economy of caregivers	Poor	68 (80.0)	17 (20.0)	0.028
	Medium, pretty rich	30 (62.5)	18 (37.5)	
Primary caregivers	Parents	80 (74.1)	28 (25.9)	0.832
	Others	18 (72.0)	7 (28.0)	
Education level of caregivers	≤ grade 9/12	71 (78.9)	19 (21.1)	0.049
	> grade 9/12	27 (62.8)	16 (37.2)	

Clinical stage	Stages III and IV		28 (87.5)	4 (12.5)	0.042
	Stages I and II		70 (69.3)	31 (30.7)	
Infectious diseases			67 (77.9)	19 (22.1)	0.135
Side effects			17 (81.0)	4 (19.0)	0.41
Immune status*		Advanced/severe immunosuppression	52 (78.8)	14 (21.2)	0.101
		Not/mild immunosuppression	35 (68.6)	16 (31.4)	
Total			98 (73.7)	35 (26.3)	

Table 5. Comparison of treatment adherence in children with HIV/AIDS with related factors.

Discussion

Epidemiological, clinical characteristics and immune status in children with HIV/AIDS

In a total of 133 children invited to participate in the study, mainly in the group of 11-15 years old (61.7%), female accounted for a slightly higher percentage than male with 57.1% and 42 respectively 9%. This result was similar to the studies of McHenry et al. and Humphrey et al. female accounted for a moderately higher proportion of 51.6% and 52.0% [10,11]. This study noted that the majority of children are Kinh ethnicity, but Khmer ethnic group, an ethnic minority, accounts for 28.6%. The reason the study was conducted in Soc Trang province is that the locality has more living characteristics of Khmer ethnic groups than other localities. Most of the children infected with HIV in the study were from poor and near-poor households with the rate of 63.9% and mainly lived in rural areas with the rate of 67.7%.

Caregivers in the study had difficulty providing optimal care for their children because most of them were unemployed and some were single parents with limited access to financial assistance. In a study by Hansen et al. that referred to the issue of "infectious diseases of poverty", describing infectious diseases that are more prevalent among poor and vulnerable populations, namely HIV infection, tuberculosis, malaria, and neglected tropical diseases [12]. HIV/AIDS remain a public health challenge in low- and middle-income countries. In this study, the primary caregivers were mainly parents (81.2%), followed by grandparents (11.3%). This result is similar to the study by Humphrey et al in western Kenya where 94% of caregivers were mothers [11]. Author Ngoc Thi et al. researched at Vietnam national children's hospital also noted that the majority of caregivers are parents and grandparents (77.6%) [13].

Among children with HIV/AIDS, 87.2% of children suffered from malnutrition; 47.2% recurrent respiratory infections; 44.1% papular pruritic eruptions; 19.5% persistent fever; 17.3% oral candidiasis, 15.7% persistent diarrhea. When a child is infected with HIV, the immune system is weakened, unable to fight off diseases, so the absorption of nutrients is also poor, creating a spiral of pathology, care and nutrition play a very important role. It is important to help children respond well to treatment, reducing the risk of opportunistic infections.

This result is similar to the study of Mc Henry et al. 50.9% were stunted, 26.5% were underweight, and 13.6% were wasted; when comparing mean z-scores, HIV + children tended to have larger and earlier dips in z-scores compared to HIV-exposed children, with significant differences found between the two groups ($p<0.001$) [10]. According to a study by Aguilera-Alonso D et al in the continental region of Equatorial Guinea, about 56.2% of children were underweight (weight-for-age ≤ 2 SD); 20.1% moderate and 36.1% severe; about 27.6% of children were underweight (weight-for-height ≤ 2 SD); 11.9% moderate and 15.7% severe; about 56.3% of children are stunted (height for age ≤ 2 SD); 20.7% moderate and 35.6% severe [14].

Most of the children in the study group were in clinical stage III (39.4%) and had advanced immunosuppression and severe immunosuppression with the rate of 25.6% and 24.1%, respectively. Aguilera-Alonso et al. also recorded 56.8% of the children studied at clinical stage III, followed by 24.9% of children at clinical stage IV; immunological stage II at 39.2% and stage III at 33.8% [14]. This result has shown the need to study the treatment adherence of children.

Adherence to treatment of children with HIV/AIDS

The overall ART adherence rate in the study was slightly low at 26.3%, mainly following side effects and opportunistic infections monitoring; clinical symptoms of tuberculosis monitoring; clinical stage follow-up; weight and height monitoring. The treatment monitoring tests were not well-performed according to the protocol: Only 47.4% of children had the first CD4 test within 15 days of being diagnosed with HIV; 69.9% of children were performed for CD4 count test and 72.2% for HIV load test periodically. This result was much lower than some other studies. The rate of overall adherence in the last month in the study of Neupane et al. was found to be 87.4% [15]. Research by Ngoc Thi Tran in Vietnam recorded an overall adherence rate of 63.0% [13]. The reason for this is because Ngoc Thi Tran's research was carried out at the outpatient clinic of Vietnam national children's hospital, the largest hospital in the country, so the monitoring and

management of patients with HIV/AIDS is stricter and more correct procedure.

Two caregiver factors associated with non-adherence to treatment were poor caregiver economics (p=0.028) and caregiver education level ≤ grade 9/12 (p=0.049). In the study by Maddock et al. in South Africa also revealed that caregiver burden was affected by available social support services and resources; financial constraints, poor access to rehabilitation and low educational attainment challenged the care provided to children with HIV/AIDS [16]. Research by Ngoc Thi Tran recognized that caregivers >50 years old are one of the important factors affecting treatment adherence [13].

Research by Verma et al. showed that adherence was the source of successful treatment outcomes and was strongly associated with the support of their parents/caregivers. The most common reason for non-compliance was forgetfulness 59%, and 57% of parents/caregivers were facing monetary issues. Long distances, longer time to get to the center and the absence of parents/caregivers are also thought to be problems [17]. This study recorded that only 44.4% of children adhered to the correct medication. Unlike adults, the use of drugs by children is very dependent on caregivers. In a study in Kabale district, south western Uganda, caregiver forgetfulness was the main cause of ART under dosing, accounting for 37% [18].

Research by Biru et al. found highlight important predictors of non-adherence. Children whose caregivers were not undergoing HIV treatment and care themselves were less likely to be non-adherent during the first week of treatment (aOR = 0.17, 95% CI: 0.04, 0.71) and the children whose caregivers did not use a medication reminder after one month of treatment initiation (aOR=5.21, 95% CI: 2.23, 12.16) were more likely to miss the prescribed dose [19]. Supporting HIV-infected people to adhere to art in the community, including taking medications as prescribed, using medication reminders, going to follow-up visits and taking tests on time; supporting patients who are late for their appointment, skip treatment, and return to the clinic on time; instructions on how to store and preserve medicines at home have been effective methods in many places. In a study in Argentina, use of mobile devices and social media was a valid tool to improve adherence to ART in HIV + infected children and young adults [20].

A important factor associated with ART non-adherence was the patient's clinical stages were stages III and IV (p=0.042). Children with clinical stage III suffered from moderate malnutrition, persistent diarrhea/fever, oral candidiasis, pulmonary tuberculosis, severe recurrent presumed bacterial pneumonia, acute necrotizing ulcerative gingivitis or stomatitis or acute necrotizing ulcerative periodontitis, anaemia (<8 g/dl) and or neutropenia (<500/mm3) and or thrombocytopenia (<50,000/mm3) for longer than one month; and children with clinical stage IV had severe wasting or severe malnutrition not adequately responding to standard therapy, recurrent severe bacterial infection, chronic herpes simplex virus infection, extra pulmonary tuberculosis, HIV encephalopathy, HIV-associated nephropathy, HIV-associated cardiomyopathy [8].

Children must take multiple drugs to treat opportunistic infections and HIV-related organ failure, so adherence to ART was limited. The care burden of children in stages III and IV with moderate/severe malnutrition and recurrent or chronic infections may further affect caregivers' ability to adhere to treatment. Consequences are easy to cause failure in the treatment of HIV. According to the study by Endalamaw et al., the combined effects of WHO clinical stage III/IV, presence of opportunistic infections and poor adherence to ART had a strong impact on HIV treatment failure. Therefore, it is necessary to have measures to diagnose HIV-infected children at an early stage.

Conclusion

Most children with HIV/AIDS in Soc Trang, Vietnam were in advanced and severe condition, while ART adherence was greatly low. Factors associated with non-adherence include the caregiver's poverty, education and the child's clinical stage. Intervention programs should focus on addressing these objects to improve the adherence to ART.

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Author's Contribution

Conceptualization: All authors; data collection, formal analysis: binh chi huynh; writing-original draft, writing-review and editing: all authors; final approval of published version: all authors.

Conflict of Interest

No existing or potential conflict of interest relevant to this article was reported.

Data Availability

The datasets generated and/or analyzed in this study are not publicly available because they are property of Can Tho University of medicine and pharmacy and Soc Trang hospital for women and children; however, they may be available from the corresponding author on reasonable request.

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