

Factors Associated with Non-Adherence to Antiretroviral Therapy among HIV-Infected Adolescents at Pediatric Department of Yopougon University Hospital, Côte d'Ivoire

Tanoh Kassi François Eboua^{1*}, Marcellin Nouaman², Marie-Hélène Ake-Assi¹, Yvette Bleu¹, Bherat Kouadio¹, Ekou Niamien¹, Laurence Adonis-Koffy¹

¹Pediatrics Department of Yopougon University Hospital, Abidjan, Côte d'Ivoire

²PAC CI ANRS Site, Abidjan, Côte d'Ivoire

Email: *ebouatk@yahoo.fr

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Abstract

Context: The consequences of non-adherence to antiretroviral therapy (ART) are harmful in terms of morbidity and mortality among HIV-infected adolescents. There is a little data in this population in West Africa, about non-adherence to ART. **Objective:** To identify factors associated with non-adherence to ART in adolescents at the Pediatric Ambulatory Treatment Center (PATC) of the pediatric department of Yopougon University Hospital. **Materials and Methods:** A cross-sectional study was conducted from May to July 2017 among adolescents aged 10 to 19 years old at PATC of pediatrics department of Yopougon University Hospital. We have considered that adolescent was not adherent to ART when he affirm that he have not taking ART at least once in the week before the survey. A logistic regression model was used to identify factors associated with non-adherence to ART. **Results:** Overall 166 adolescents were included. The median age was 15 years old [IQR = 13 - 17 years]. They had a detectable viral load greater than 1000 copies/ml in 41.8% of cases. The rate of non-adherence to ART was 40.4%. The factors associated with non-adherence to ART were male [OR = 2.5 (CI = 1.1 - 10.0)], having parent widowed [OR = 7.8 (CI = 1.6 - 39.3)] or divorced [OR = 3.7 (CI = 1.1 - 13.5)], CD4 inclusion rate \geq 500 cells/ml [OR = 8.5 (CI = 1.6 - 45.5)] and duration on ART \geq 10 years [OR = 8.9 (CI = 1.6 - 50)]. **Conclusion:** A rigorous therapeutic education taking into account associated factors in this study is necessary to reduce the rate of non-adherence among adolescents at PATC.

Keywords

Adolescent, Adherence, Antiretroviral Treatment, Cote d'Ivoire

1. Introduction

Significant progress has been made in the fight against HIV infection since the advent of this pandemic. In fact, between 2000 and 2016, the number of new infections fell by 39% and the number of HIV-related deaths fell by a third. Access to antiretroviral treatment (ART) has saved 13 million of life in the world [1] [2]. This access to ART has resulted in better survival of HIV-infected children who reach adolescence [3]. Adolescents are a vulnerable population. Many physical and emotional changes normally occur during adolescence and many factors can compromise their adherence to ART [4].

Since 2013, to put an end to AIDS epidemic, UNAIDS recommends that 90% of people living with HIV know their HIV serologic status, that 90% HIV infected people receive sustainable ART and that 90% of people receiving ART have viral suppression load by 2020 [5]. To achieve the third target of the UNAIDS target (virological suppression), good adherence to ART is indispensable. Adherence to ART remains a challenge in the care of adolescents living with HIV [6] [7] [8] [9]. Therapeutic failure is a consequence of poor adherence to ART. It will cause persistence of viral replication. And if nothing is done we will observe the emergence of resistance to ART objectified by genotypic tests of resistance to antiretroviral molecules [9] [10] [11]. There is little data in West Africa, about non-adherence to ART among HIV-infected adolescents. In order to undertake effective actions to minimize the consequences of non-adherence in HIV-infected adolescents, it is necessary to identify the barriers to ART adherence. The objective of this study was therefore to identify the factors associated with ART non-adherence in adolescents attending at the Pediatric Ambulatory Treatment Center (PATC) of the pediatric department of Yopougon University Hospital.

2. Materials and Methods

A cross-sectional study was conducted at the PATC of the pediatric department of Yopougon University Hospital from May to July 2017. Adolescents aged 10 to 19 years old on ART followed for at least 6 months and with updated biological status were included (viral load, CD4 count). Adolescents with severe progressive illness (requiring hospitalization) the day of the survey were excluded. We have selected a convenience sample of adolescents attending at PATC. Eligible adolescents were systematically interviewed using a standardized questionnaire administered face-to-face during the consultation to assess the level of non-adherence. An adherence counseling has been initiated for adolescents who have not good adherence to ART (about difficulty to take ART, management of drugs adverse and reasons of difficulty of adherence to ART). Sociodemographic data (age, sex, educational level, type of housing, marital status of parents, vital status of parents), clinical data (clinical stage of the CDC), biological data (viral load and CD4 lymphocyte count) and therapeutic data (ART regimen, duration of on ART) were collected from the patient records. The clinical stage at inclu-

sion was evaluated according to the staging of the CDC Atlanta and the level of immune depression according to the WHO classification. To define adherence to antiretroviral treatment we considered the definition of the national guide to pediatric care for HIV infection [12]. Good adherence is estimated at 90 to 95%. So in our study, at least one missed ART intake in the previous week the survey was considered to define non-adherence to ART. Logistic regression was used to identify factors associated with non-adherence to ART. Odd-ratio were estimated with their 95% confidence intervals. A p-value < 0.05 was considered statistically significant. Statistical Analyzes were done with Stata software (Stata™ 12.0 College Station, Texas, USA).

3. Results

3.1. Characteristics of the Study Population

Overall, 449 HIV-infected children on ART are followed at PATC. Of them, 310 adolescents are between 10 and 19 years old. In this study 166 was included. The median age was 15 years (IQI = 13 - 17). The sex ratio was 1. Adolescents with a Secondary or higher education level accounted for the majority of the sample (74.7%). They lived in a common court or in individual housing respectively in 36.5% and 63.5% of cases. They came from parents who were married (57.1%), divorced or separated (22.9%) and widowed (20%). They were fatherless in 24.2% and motherless in 29.3% of cases. At baseline, adolescents had CDC clinical stage A, B, and C respectively in 48.2%, 38.6% and 13.2% of cases.

They had severe immunosuppression at baseline (CD4 count \leq 200 cel/mm³) in 15.1% of cases.

Undetectable viral load was found in 43.0% of cases. They had a viral load less than 1000 copies in 14.6% of cases. The antiretroviral regimen was based on zidovudine, tenofovir and lopinavir, respectively, in 54.8%, 39.2% and 2.4% of cases. The average duration of ART was 10 years.

Table 1 and **Table 2** show the distribution of adolescents by level of adherence to ART.

3.2. Factors Associated with Non-Adherence to ART

Factors associated with non-adherence to ART are shown in **Table 3** and **Table 4**.

In multivariate analysis, the factors associated with non-adherence to ART were sex, marital status of parents, baseline CD4 count, and duration of antiretroviral therapy. Girls were less likely to be non-adherence to ART than boys [OR = 0.4 (95% CI = 0.1 - 0.9)]. Adolescents with separated or divorced parents [OR = 3.7 (95% CI = 1.1 - 13.5)] and adolescents with widowed parents [OR = 7.8 (95% CI = 1.6 - 393)] were more likely to be non-adherent to ART.

Adolescents with no immune deficiency (CD4 count > 500 cel/mm³) had a higher risk to be non-adherent to ART [OR = 8.5 (95% CI = 1.6 - 45.5)]. A duration on ART more than 10 years in adolescents increased the risk of being non-adherent.

Table 1. Sociodemographic characteristics of adolescents according to adherence to ART, n = 166.

Socio-demographic variable	Adherence N (%)	Non-adherence N (%)	Total n (%)	p
Median age (IQI) (years)	16 (13 - 17)	15 (13 - 17)	15 (13 - 17)	
Level of education				0.97
Never schooled	2 (2.0)	1 (1.6)	3 (1.8)	
Primary	23 (23.5)	15 (23.4)	38 (23.5)	
Secondary/Higher	73 (74.5)	48 (75.0)	121 (74.7)	
missing	1	3	4	
Type of dwelling				0.98
Common court	33 (36.7)	23 (36.5)	56 (36.6)	
Individual housing	57 (63.3)	40 (63.5)	97 (63.4)	
missing	9	4	13	
Marital status of parents n = 111				0.37
Live as husband and wife/married	40 (57.1)	18(43.9)	58 (52.3)	
Divorced/separated	16 (22.9)	11(26.8)	27 (24.3)	
Widowed	14 (20.0)	12 (29.3)	26 (23.4)	
Missing	29	16	55	
Vital status of mothers				0.25
Alive	70 (70.7)	41 (62.1)	111 (67.3)	
Dead	29 (29.3)	30 (37.9)	54 (32.7)	
Missing	0	1	1	
Vital status of father				0.01
Alive	75 (75.8)	38 (56.7)	113 (68.1)	
Dead	24 (24.2)	29 (43.3)	53 (31.9)	
Father/Mother Couple n = 165				0.02
Alive	91 (91.9)	53 (80.3)	144 (87.3)	
Dead	8 (8.1)	13 (19.7)	21 (12.7)	
Missing	0	1	1	

Table 2. Clinical, immune-virological and therapeutic characteristics according to adherence to ART, n = 166.

Clinical, biological and therapeutic variable	Adherence n (%)	Non-adherence n (%)	Total n (%)	p
CDC Clinical stage				0.12
Stage A	52 (52.5)	28 (41.8)	80 (48.2)	
Stage B	34 (34.3)	30 (44.8)	64 (38.6)	
Stage C	13 (13.2)	9 (13.4)	22 (13.2)	
CD4 inclusion rate				0.05
≤200	19 (19.2)	6 (9.0)	25 (15.1)	
200 - 500	27 (27.3)	19 (28.4)	46 (27.7)	

Continued

>500	53 (53.5)	42 (62.6)	95 (57.2)	
Viral load				0.16
Undetectable	45 (47.9)	28 (38.9)	73 (44.0)	
<1000 copies	20 (21.3)	4 (5.6)	24 (14.5)	
>1000 copies	29 (30.8)	40 (55.5)	69 (41.5)	
ARV regimen n = 160				0.16
AZT...	57 (60.6)	34 (51.5)	91 (56.9)	
TDF...	34 (36.2)	31 (47.0)	65 (40.6)	
...LPV/r	3 (3.2)	1 (1.5)	4 (2.5)	
Missing	5	1	6	
Daily ART dose				0.42
Single-dose	48 (49.0)	30 (46.2)	78 (48.0)	
Multi-dose	50 (51.0)	35 (53.8)	85 (52.0)	
Missing	1	2	3	
Galenic form of ART				0.40
Dispersible tablets	8 (9.2)	1 (1.6)	9 (6.0)	
Dry tablets	74 (85.1)	56 (90.3)	130 (87.2)	
Dry tablets + dispersible tablets	5 (5.7)	5 (8.1)	10 (6.8)	
Missing	12	5	17	
Duration on ART (years)				0.03
0 - 5	27 (29.3)	10 (15.6)	37 (23.7)	
0 - 10	37 (40.2)	25 (39.1)	62 (39.7)	
>10	28 (30.5)	29 (45.4)	57 (36.6)	
Missing	7	3	10	
Help in taking ART n = 161				0.41
Mother	37 (38.5)	23 (35.4)	60 (37.3)	
Father	16 (16.7)	7 (10.8)	23 (14.3)	
Father and mother	10 (10.4)	10 (15.4)	20 (12.4)	
All family members	23 (24.0)	18 (27.7)	41 (25.5)	
Other	10 (10.4)	7 (10.7)	17 (10.5)	
Missing	3	2	5	

Table 3. Sociodemographic factors associated with non-adherence to ART.

Socio-Demographic Variable	Univariate analysis		Multivariate analysis	
	n/N	OR (CI 95%)	p	OR (CI 95%) p
Sex			0.63	0.04
Male	35/83	1		1
Female	32/83	0.7 (50.4 - 1.6)		0.4 (0.1 - 0.9)
Age (years)			0.68	
≤13	18/50	1		

Continued

13 - 18	34/83	1.2 (0.6 - 2.5)		
≥18	15/33	1.5 (0.6 - 3.6)		
Level of education				0.97
Never schooled	01/03	1		
Primary	15/38	1.3 (0.1 - 15.6)		
Secondary/higher	48/121	1.3 (0.1 - 14.9)		
Type of dwelling				0.98
Common court	23/56	1		
Individual housing	40/97	1.1 (1.2 - 4.6)		
Vital status of father				0.01
Alive		1		
Dead		2.4 (1.2 - 4.6)		
Vital status of mothers				0.25
Alive	38/113	1		
Dead	29/53	1.5 (0.7 - 2.8)		
Father/mather couple				0.03
Alive	53/144	1		
Dead	13/21	2.8 (1.1 - 7.2)		
Marital status of parents				0.16
Live as husband and wife/married	18/58	1		1
Divorced/separated	11/27	1.5 (0.6 - 3.9)		3.7 (1.1 - 13.5)
Veuf/veuve	12/26	1.9 (0.7 - 4.9)		7.8 (1.6 - 39.3)
Person supporting adolescent				0.08
Mother	18/44	1		
Father	08/24	1.4 (0.5 - 3.9)		
Father and motherr	14/46	0.8 (0.3 - 2.5)		
Other	22/37	2.9 (1.0 - 8.5)		

Table 4. Clinical, biological and therapeutic Factors associated with non-adherence with ART.

Clinical, biological and therapeutic variable	Univariate analysis			Multivariate Analysis	
	n/N	OR (CI 95%)	P	OR (CI 95%)	P
CDC Stage at inclusion			0,32		
Stage A	28/80	1			
Stage B	30/64	1.6 (0.8 - 3.2)			
Stage C	09/22	1.3 (0.5 - 3.4)			
CD4 inclusion rate			0.09		0.02
<200	06/25	1		1	
200 - 500	19/46	2.2 (0.7 - 6.6)		3.5 (0.6 - 20.0)	

Continued

>500	42/95	2.5 (0.9 - 6.8)	8.5 (1.6 - 45.5)	
Viral load				
Undetectable	45/73	1		
<1000 copies	20/24	1.2 (0.5 - 2.5)		
>1000 copies	29/69	1.6 (0.9 - 3.0)		
ARV Regimen				0.39
AZT...	34/91	1		
TDF....	31/65	1.5 (0.3 - 1.2)		
...LPV/r	01/04	0.5 (0.1 - 5.6)		
Galenic Form				0.09
dispersible tablets	01/09	1		
Dry tablets	56/130	6.1 (0.7 - 49.8)		
Dry tablets + dispersible tablets	05/10	8.0 (0.7 - 90)		
Daily ARV dose				0.72
Single-dose	30/78	1		
Multi-dose	35/85	1.1 (0.6 - 2.1)		
Duration on ART (years)				0.02
0 - 5	10/37	1	1	
5 - 10	25/62	1.8 (0.7 - 4.4)	3.8 (0.9 - 17.1)	
>10	29/57	2.8 (1.1 - 6.8)	8.9 (1.6 - 50.2)	

4. Discussion**4.1. Adherence to ART**

This study specified the rate of non-adherence and the factors associated with non-adherence to ART in adolescents at the PATC of pediatric department of Yopougon University Hospital.

Good adherence to ART in HIV-infected adolescents is essential to achieve virological suppression. Actually adherence to ART in HIV-infected adolescents remains problematic [4].

The rate of non-adherence to ART is high in this study (40.4% of 166 adolescents interviewed). Because of the method used in this study, we would have expected a lower rate. In fact, the self-assessment method of the compliance measure may overestimate the ART adherence rate [13]. To minimize this information bias parents and adolescents have been reassured during obtaining consent. Several studies in adolescents have shown rates of non-adherence to ART between 20% and 35% [14] [15] [16] [17]. Other study in North America and Spain among adolescents and adults estimated the non-adherence rates at 45% and 43% [18] [19]. It has been shown that the variation in the rate of non-adherence to ART observed in the studies is related to the use of evaluation method [17] [18].

4.2. Factors Associated with Non-Adherence to ART

Our study has identified epidemiological, social and biological factors associated with non-adherence to ART. Girls were likely to be less non-adherent than boys.

This result was also found in a study conducted in Zambia among 15 - 19-years old adolescents [20]. However, other studies have shown no significant difference between girls and boys [21]. This difference in the rate of non-adherence to ART between girls and boys HIV infected varies from one region to another. The environment in which these adolescents live might explain this difference. A qualitative study was necessary to explain this difference of adherence to ART in girl and boys adolescents HIV-infected.

Also, adolescents from divorced, separated, or widowed parents had a higher risk of being non-adherent to ART. In fact, a stable family environment in the presence of the biological parents would be a favorable environment to promote a better adherence to ART. Several studies have found that the presence of a biological parent is a factor frequently associated with good adherence to treatment [22] [23].

The absence of immune depression implying a non-advanced clinical state of the disease is a risk factor for non-adherence to ART in our study. Many studies have shown that in the early stage of the disease, adolescents are less likely to adhere to treatment [24] [25] [26]. These adolescents in relatively healthy do not find need to take their drugs. A study conducted in Uganda showed that patients hospitalized at least twice and therefore symptomatic were more likely to adhere to ART [27]. There is evidence that the level of adherence tends to decline over time in adolescents on ART and tiredness has often been the reason for non-adherence to ART in adolescents living with HIV in Uganda [28]. In our study, a duration of ART beyond 10 years increased the risk of being non-adherent at ART.

Regular compliance counseling and rigorous therapeutic education are needed to minimize the risk of non-adherence in these adolescents who are already weakened by their physical, emotional and psychological state.

5. Conclusion

This study shows that the level of ART non-compliance among adolescents at the Pediatric Ambulatory Treatment Center of the pediatric department of Yopougon University Hospital is high. Males, adolescents from divorced, separated or widowed parents, lack of immune depression at baseline, and duration of ART beyond 10 years were the main factors associated with non-adherence to ART. Regular compliance counseling and rigorous therapeutic education are needed to minimize the risk of non-adherence. Observational cohort studies need to be undertaken to better understand the determinants of non-adherence to ART in West Africa.

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Competing Interests

The authors declare that they have no competing interests whether financial or any other.

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