24-month clinical, immuno-virological outcomes and HIV status disclosure in adolescents living with perinatally-acquired HIV in the COHADO cohort, in Togo and Côte d'Ivoire, 2015-2017

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Abstract

Background: Adolescents living with perinatally-acquired HIV (APHIV) face challenges including timely disclosure of their HIV-serostatus that was explored in the West-African COHADO cohort. We assessed the 24-month outcomes in COHADO, among APHIV in relation to the disclosure of their own HIV-serostatus.

Methods: Nested within the International epidemiologic Database to Evaluate AIDS pediatric West African prospective cohort (IeDEA pWADA), the COHADO cohort included antiretroviral (ART)-treated APHIV aged 10–19 years, enrolled in HIV-care <10 years, in Abidjan (Côte d'Ivoire) and Lomé (Togo) in 2015. A favorable 24-month outcome was defined when combining being retained in care, without progression to WHO-AIDS stage, with CD4 cell count > baseline CD4 ($\pm 10\%$) and with virological suppression (viral load [VL] <50 copies/mL). We investigated correlates of APHIV favorable 24-month outcome using multivariate logistic regression.

Results: Overall, 209 APHIV were included, 51.6% in Abidjan, 54.5% were females. At inclusion, median CD4 cell count was 521/mm³ (IQR[281-757]); only 29.6% had a VL measurement of whom 3.2% in virological suppression. APHIV were younger in Lomé (median age: 12 years (interquartile range [IQR]:11-15) compared to Abidjan (14 years (IQR:12-15, $p=0.01$)). Full HIV-disclosure increased from 41.6% at inclusion to 74.1% after 24 months. After 24 months of follow-up, 6 (2.9%) died, 8 (3.8%) were lost to follow-up, 4 (1.9%) were transferred out. Overall, 73.7% did not progress to WHO-AIDS stage, 62.7% had CD4 count above ($\pm 10\%$) of the baseline value (48.6% in Abidjan versus 69.0% in Lomé, $p<0.001$). Among the 83.7% with VL measurements, 48.8% were in virological suppression (Abidjan: 45.4%, Lomé: 52.5%, $p<0.01$). The 24-month combined outcome was favorable for 45% (29.6% in Abidjan and 61.4% in Lomé, $p<0.01$). Adjusted on sex, age, a 24-month favorable outcome was not associated with HIV-disclosure status but was significantly higher for APHIV living in Lomé compared to those living Abidjan (adjusted odds ratio =4.41, 95%CI:2.29-8.50).

Conclusions: 24-month favorable outcome rates were low among West-African APHIV and differed across countries. HIV-disclosure frequency improved over time but remained low. Context-specific responses are urgently needed to improve adolescent's care to reach the UNAIDS 90% target of virological success for those on ART.

Introduction

Access to antiretroviral therapy (ART) in sub-Saharan Africa has significantly expanded since 2004 [1]. As a result, children living with perinatally-acquired HIV are those HIV-infected through the mother-to-child mode of transmission at any (in utero, during delivery or post-natally through breastfeeding) and are now growing up into adolescence. The critical period of adolescence is characterized by biological, psychosocial changes in a context where HIV disease is turning into a chronic condition [2, 3]. Globally, 1.8 million adolescents aged 10–19 years were living with HIV in 2017 [4]. Sub-Saharan Africa is the most impacted region, accounting for 84% of adolescents living with HIV (ALHIV) [4–6]; adolescent girls

accounted for three-quarters of all new HIV infections among adolescents in 2018 [7]. HIV/AIDS was the leading cause of death amongst adolescents in this region in 2016 [8]. Among the 23 African priority countries, AIDS-related deaths estimated were 24 000 [17 000–33 000] from adolescents aged 10–14 years and 25 000 [18 000–34 000] among adolescents aged 15–19 years in 2017 [9]. Despite the progress achieved in pediatric HIV care, attention must be paid to the expanding population of adolescents living with either perinatally or non-perinatally acquired HIV, since it is estimated that new HIV infections in adolescents will increase 13% annually by 2030 in Africa [10, 11]. This is particularly true in West and Central Africa, which has recorded a 35% increase in the annual number of AIDS-related deaths among adolescents aged 15-19 years from 2010 to 2016 [12].

Since 2015, universal ART is recommended by WHO [13]. Compared to adults or younger children, adolescent living with perinatally acquired HIV (APHIV) experience higher morbidity, mortality and lower rates of virological suppression on ART [3, 14–16]. This is most likely related to delayed access to HIV diagnosis and ART in childhood, lack of timely HIV-disclosure while growing-up, with poor medication adherence in a context of prolonged ART, poor retention in care, explained by individual, social, and structural barriers [6, 17–21]. Transition to adult care also remains a vulnerable step in ALHIV care [22, 23]. All these factors contribute to delaying the UNAIDS' 90-90-90 targets of ALHIV's cascade of care meaning that 90% of ALHIV living with HIV are knowing their HIV status, 90% of those infected are on ART and 90% of those on ART are achieving virological suppression by 2020 [24].

However, timely HIV-disclosure in APHIV is a crucial step to motivate them to adhere to ART and to achieve this 90-90-90 UNAIDS targets [21, 24]. The full-disclosure of an HIV diagnosis includes naming HIV/AIDS, provide information about care and the modes of transmission HIV disease [21]. Unfortunately, a large proportion of APHIV diagnosed during their infancy, remain unaware of their own HIV-positive status while they are growing-up. In many African pediatric sites, even if children or adolescents on ART, healthcare providers and caregivers delayed their HIV-disclosure because of cultural factors, the lack of national guidance [21]. Caregivers are also not ready, and fear their adolescent will disclose the family secret with subsequent stigma [25–28]. According to a previous review, 1.7% to 41% of children and ALHIV in low and middle-income countries are fully disclosed of their HIV-positive status [29]. In West-Africa, less than a third of APHIV knew their status in 2011 and the HIV-disclosure process often occurs late, after the WHO-recommended age of 12 years [30, 31]. Data suggested that an earlier full HIV-disclosure could improve ALHIV outcomes through improved ART adherence, retention in care and slower disease progression [28, 32, 33].

The prospective monitoring of the HIV-disclosure process in APHIV is crucial to understand their clinical, immunological and virological long-term outcomes. To better document outcomes of APHIV in West Africa, the COHADO ("COHort of ADOlescents living with HIV") sub-cohort, as part of the West African International epidemiologic Database to Evaluate AIDS (leDEA) pediatric cohort Collaboration, was launched in 2015 in two sites of the West-African leDEA pediatric cohort in Lomé (Togo) and Abidjan (Côte d'Ivoire). This study is aimed to better document the HIV-disclosure frequency and its process over

24 months in relation with 24-month health outcomes among APHIV since inclusion in the COHADO cohort.

Methods

Study design

The leDEA pediatric West African Database to evaluate AIDS (pWADA) is an international multicentric prospective cohort as part of the leDEA global pediatric collaboration (<https://www.iedea.org/>) supported by the US National Institutes of Health since 2006, to describe HIV epidemiology trends and evaluate HIV outcomes using large patient-level observational databases. It included children and adolescent (< 16 years of age) living with HIV from 11 pediatric clinical centers in seven West African countries (Benin, Burkina Faso, Côte d'Ivoire, Ghana, Mali, Senegal and Togo). It aimed at addressing HIV/AIDS research questions regarding HIV care and outcomes in children and adolescents living with HIV in West Africa [34]. Nested in pWADA, the COHADO prospective cohort was aimed at collecting prospective data to focus on ALHIV specific issues such as the HIV-disclosure process and behavioral issues in Lomé (Togo) and Abidjan (Côte d'Ivoire) between 2015 and 2017.

Settings and study population

The COHADO cohort included APHIV from the pediatric pWADA active file of the Teaching Hospital of Yopougon (Abidjan, Côte d'Ivoire) and the Sylvanus Olympio Teaching Hospital (Lomé, Togo). In accordance with national guidelines, APHIV followed up in these sites were typically seen in medical consultation quarterly. CD4 count were measured six-monthly, and since 2016, viral load was monitored on a yearly basis.

Between January 2015 and November 2015, ART-treated ALHIV aged 10–19 years, included in HIV-care before the age of 10 years (as a proxy of perinatal infection in the absence of know mode of transmission), and followed up in the two participating sites, were invited to participate in the study.

Data collection

Study-specific data including living and schooling condition, parents' vital status, access to running water, access to electricity, disclosure (at baseline and during follow-up) and disclosure process, were recorded using standardized questionnaires assessed yearly. Other sociodemographic, clinical and therapeutic data were extracted from medical records and from the leDEA pediatric central database.

HIV-disclosure process data (disclosure status, date of full disclosure, person in charge of disclosure) were recorded from parents/legal guardian to avoid any accidental HIV-disclosure to the adolescent

during the interview. HIV-disclosure was defined as full disclosure when the APHIV has been told that he or she has HIV/AIDS specifically, and he/she knew the care and the modes of transmission [21].

Treatment adherence was evaluated by the counsellor, using the ratio between the number of pills prescribed and the number of pills taken during the four days preceding the visit. Good treatment adherence was defined as more than 95% of planned doses taken.

Data analysis

Baseline was defined as the date of inclusion in the COHADO cohort. Our endpoint, a 24-month favorable outcome, was measured at the 24-month visit combining multiple criteria: (i) vital status (alive, died, lost to follow-up); (ii) clinical criteria (WHO clinical stage [35] evolution from baseline); (iii) immunological criteria (difference in CD4 count since baseline); (iv) virological criteria (HIV viral load). APHIV was defined as lost to follow-up if s/he did not report for any follow-up for at least 6 months, and for whom transfer, or vital status was unknown.

After describing each criterion separately, we assessed a combined outcome pooling all criteria at 24 months. A favorable combined outcome was defined as being alive and followed up without progression to WHO AIDS stage; having a CD4 cell count above the baseline value ($\pm 10\%$) and being in virological suppression (viral load < 50 copies/mL). APHIV with missing data in one of the evaluation criterion were classified using the other criterion and we performed sensitivity analyses.

We described APHIV baseline characteristics using median values with inter-quartile ranges (IQR) for continuous variables and proportions for categorized variable, globally and by site. Full HIV-disclosure was assessed over the 24 months of follow-up: APHIV were classified as non-disclosed, disclosed to during the past 2 years (after inclusion in COHADO), and disclosed to >2 years, thus before inclusion in COHADO (for them, the timing of disclosure was often not recorded).

We described 24-month outcomes overall, according to site, disclosure status and other baseline characteristics. Correlates of favorable combined outcome in COHADO at 24 months of follow-up were investigated using a backward stepwise logistic regression analysis, including all co-variables significantly associated at a 20% threshold in the univariate analyses. Age and sex were forced in the final multivariate model. We tested for country-specific practices adding an interaction between disclosure and country, but this was non-significant. All analyses were performed using STATA 14.2 (Statacorp, College Station, TX, USA).

Results

Selection and inclusion of ALHIV in the COHADO cohort

From January 2015 to November 2015, 511 ALHIV visited the sites of Abidjan and Lomé. Among them, a total of 209 (40.9%) APHIV were offered enrolment in COHADO and gave their consent (Figure 1). Reasons for not being included were mainly due to either refusal of parents and APHIV, or the low availability of health care workers to propose participating in the study, due to over workload. ALHIV included in COHADO did not differ from others who visited the sites in terms of sex, age and immunological status distributions at baseline. However, there were high rates of missing data for both WHO clinical staging and viral load data (Table 1).

Baseline characteristics

Baseline characteristics are presented in Table 2. Among the 209 APHIV included, 51.7% (n=108) lived in Abidjan and 54.6% (n=114) were female. Median age was 13 [IQR: 11-15] years; APHIV were significantly older in Abidjan compared to Lomé (p=0.01). The APHIV median ART duration prior to inclusion in COHADO was 6 [IQR: 4-10] years and it was significantly longer in Abidjan than in Lomé (p<0.01).

Only 23.9% of the cohort lived with both biological parents. Most APHIV (89.9%) were from urban areas, 97.1% had access to electricity and 62.7% had access to piped drinking water at home.

Overall, 17.2% had already reached the WHO AIDS stage 4 at baseline, this proportion was higher in Lomé (32.7%) compared to Abidjan (2.8%) (p<0.01). Regarding ART, 81.2% were on an NNRTI-based regimen, and 56.4% of APHIV were good adherent to ART, as defined in the methods section. Only 29.6% of APHIV had a viral load measurement, of whom 3.2% reached virological suppression (<50 cp/mL).

At baseline, 41.6% were already fully disclosed of their HIV-serostatus, this proportion was significantly higher in Abidjan (57.4%) compared to Lomé (24.8%, p<0.01).

24-month outcomes

Among the 209 APHIV, 32.5% were HIV-disclosed over the 24-month follow-up period, reaching a proportion of 74.1% who were fully HIV-disclosed at endpoint (+78.1% compared to baseline, p<0.01). During follow-up, the increase in HIV disclosure frequency relatively to baseline was stronger in Lomé (+52.5%) than in Abidjan (+13.9%) (p<0.01). (Table 3)

By 24 months, six APHIV had died (2.9%) and eight were lost to follow-up (3.8%). Among the 209 APHIV, the 24-month combined outcome was favorable for 45% of APHIV. The proportion of APHIV with a favorable outcome was higher in Lomé (61.4%) compared to Abidjan (29.6%, p<0.01) (Table 3).

HIV disclosure process characteristics

The APHIV informed of their own HIV-serostatus at the endpoint were significantly older (median age: 16 [IQR: 14-18] years) than those not informed (median age: 13 years [IQR: 12-14]) ($p < 0.01$). These APHIV also tended to be more advanced in HIV disease and had significantly lower median CD4 cell (22.6% at WHO stage 4/AIDS; CD4 cell count: 508 cells/mm³ [IQR: 348-750]) compared to those not disclosed to (14.8% at WHO stage 4/AIDS; CD4 cell count: 596 cells/mm³ [IQR: 455-871]) (Table 4).

Questioned about the reason of non-disclosure at baseline, parents/legal guardians of the 122 APHIV unaware of their HIV-serostatus declared fear of the adolescent's reaction (75.0%) and fear of HIV status divulgation to others (69.1%) as the most frequent reasons. Other reasons included the young age of APHIV (52.9%) and the fact that parents were also not prepared (35.3%).

Among the 155 APHIV who were fully HIV-disclosed to by last contact, both parents (40.7%) and psychologists (54.2%) were the most involved in the HIV disclosure process; at the contrary, doctors have very little involvement in the process, only 5.2% of APHIV (Table 5).

Factors associated with a favorable 24-month combined outcome

Table 6 presents the correlates of a 24-month favorable combined outcome in APHIV. In the univariate analysis, we found that APHIV from Lomé (vs Abidjan), without access to piper water (vs with access to piper water) and with baseline WHO clinical stage 4 (vs WHO clinical stage 1,2,3) were significantly more likely to have a 24-month favorable outcome. Contrariwise, being an orphan tended to reduce the odds of a 24-month favorable outcome, but this was not significant.

In the final model, adjusted for sex, age and disclosure status, APHIV disclosure status was not associated with having a favorable 24-month outcome (Disclosed $\leq$ 2 years since baseline: adjusted odds ratio (aOR)=0.50, 95%CI [0.21-1.15], $p=0.10$; Disclosed >2 years since baseline: (aOR)=0.65, 95%CI [0.25-1.72], $p=0.39$) (Table 6). APHIV from Lomé were four times more likely to have a favorable 24-month outcome compared to those from Abidjan (aOR: 4.41, 95%CI [2.29-8.50]).

We performed sensitivity analyses for APHIV with 24-month outcomes defined with one missing criterion, the result remained similar, with no significant effect of disclosure.

Discussion

For the first time to our knowledge, this cohort reports a snapshot on the clinical, immunological and virological outcomes of APHIV measured over 24-month in relation to HIV-disclosure in two West African pilot sites contributing to the leDEA West Africa collaboration. We made several key findings: first, the COHADO project has encouraged the full HIV-serostatus disclosure to APHIV, with an increase from 46.1% to 74.1% after 24 months, but we still found that one in four APHIV remained not formally disclosed of his/her own HIV-serostatus at the endpoint while they all were aged above 13 years. Second, unlike the

caregivers and the psychologists, doctors have very little involvement in the disclosure process. Third, we found that those APHIV disclosed to were at a more advanced stage of the disease than those unaware of their status. Fourth, after 24-month of follow-up, the cumulative death rate was high, close to 3%, and only 45% of APHIV had a favorable 24-month combined outcome after two years of follow-up. Finally, adjusted on sex, age, the HIV disclosure status was not associated with the outcome, but strongly with the site context: APHIV from Lomé increased by four the odds of a favorable 24-month outcome compared to those from Abidjan.

Although the frequency of ALHIV fully disclosed of their HIV-serostatus varies according to studies in Africa, it remains overall low ranging from 16% to 39% [36–41]. In our study, we found that only 46.1% knew their HIV status at baseline, and 74.1% by 24 months of follow-up. Although this should be closer to 100% according to the WHO recommendations, this is higher than reported in previous studies, particularly for West Africa [25, 31, 42]. In Ghana, two separate studies reported the proportion of HIV disclosure to be 11.2% among children and adolescents aged 8-14 years in 2009 and 44% among ALHIV aged 12 -19 years in 2015 [25, 43]. Furthermore, we observed an increase in the HIV-disclosure process over the 24-month follow-up period. This is clearly visible in Lomé where the proportion of APHIV disclosed had increased from 24.8% to 77.2%. One of our hypothesis is that likely occurred after a 3-day training workshop on HIV-serostatus disclosure to ALHIV delivered in 2016, in Abidjan and involving the HIV health professionals from all the leDEA-pWADA sites [44]. This workshop may have changed the health care workers' practices regarding disclosure and explain the significant increase of HIV-disclosure rate at the endpoint, but we also acknowledge that this is can be only correlated to the adolescent age.

As a matter of fact, we found that few doctors are involved in the process of HIV-disclosure, and they tended to delegate the disclosure practice to others for several reasons including over clinical work load, or fear in doing it. Indeed, healthcare workers face structural issues including limited human and technical resources, whereas disclosure is a complex process which needs time and training [21, 28]. In 2018, there were too few counselors working in the current HIV-programs. Thus, when existing in the HIV-programs, psychologists are better trained to address mental issues such as HIV-related stigma and taboo, explaining their good in the process. But they became the only person being in charge in the full HIV-disclosure process and they are not always daily available. Therefore, we feel that the whole staff should be involved in the HIV-disclosure with a multidisciplinary approach and task-sharing. That approach should be set-up at each HIV program level to offer a comprehensive care, including the process of HIV status disclosure. It is important for national and regional programmes, to tailor locally appropriate strategies to improve disclosure practice, such as the training of multidisciplinary team on disclosure mentioned earlier [34]. Furthermore, caregivers are also unprepared for disclosure and fear ALHIV stigmatization. For many parents, children are too young or are not ready to receive HIV-disclosure [26, 29, 45]. The role and benefits of having caregivers involved in the HIV disclosure process remain unclear. While some studies have suggested that caregivers are in a much better position to disclose ALHIV serostatus, others have reported that according to ALHIV, health workers are better placed [46–48].

Nevertheless, a better understanding of what refrain caregivers to disclose their HIV-status to their child is important to support them accordingly.

We found that APHIV disclosed of their HIV status tended to have worse immunological and clinical condition than those not disclosed. Unfortunately, we were not able to assess the exact timing of HIV disclosure as this is an evolving process that can take several clinical visits. We make however, two main hypotheses that could explain this observation. Either HIV disclosure had a negative effect on the APHIV leading to poor ART adherence and thus poor clinical outcomes. Or, it is the poor immunological and clinical condition of the patient that led to HIV-disclosure, in order to improve urgently their health condition via the improvement of their adherence to ART. We feel, in the context of our study, that this second hypothesis is most likely. This indication bias could have reduced the disclosure effect measured at the 24th month, since APHIV disclosed have worse health conditions. We also noted that those disclosed to were significantly older, and therefore most likely to be at a more advanced stage of the disease. Previous cohort studies, in both high and low income settings have reported that younger age of APHIV is associated with less frequent WHO 4 clinical stage compared to older APHIV [49, 50].

During follow-up, the cumulative death rate reached 3%. While this seems high, it is lower than that reported in other studies conducted in ALHIV in sub-Saharan Africa, where it ranged from 4-6% [33, 51]. Although these rates remain in the same order of magnitude, our lower rate could be explained by the shorter follow-up duration.

Overall, 45% of APHIV had favorable combined 24-month outcome; this was more frequent in Lomé than in Abidjan. However, APHIV in Lomé were in poorer clinical and immunological condition compared to those from Abidjan, and therefore had more leeway to reach a favorable 24-month outcome. Although, we were not able to document different sub-types, we do not support a difference between the two sites to explain the difference. Our finding highlights rather differences of care practices and resources available between West African cities, which must be considered to improve APHIV care. Nevertheless, our outcomes are observed in the context where about 80% of APHIV were receiving a NNRTI-therapy with a limited access to second-line therapy, common in West-Africa. The sub-optimal virological response in our population is in line with the results reported in a snapshot-study conducted in Lomé in 2016, with high rates of virological failure and drug resistance [16].

Many studies have reported on how HIV disclosure improves ALHIV clinical, immunological and virological outcomes as well as retention in care[28, 32, 33, 51, 52]. In COHADO, we found that HIV disclosure tend to reduce the odds of having a favorable 24-month outcome, though this was not significant. This result could partially be explained by the disclosure indication bias induced in COHADO, previously mentioned, where disclosure is prompted by the advanced stage of the disease. We advise caution in the interpretation of this observation. Because the disclosure variable was not standardized, nor we did not have the date of disclosure for all APHIV. A substantial proportion of APHIV was indeed disclosed before inclusion in COHADO cohort and without disclosure date. So, the association between

disclosure and the 24-month favorable outcome is evaluated at a time too soon for some APHIV and too far for others.

It has been previously reported that ALHIV non-disclosure of HIV-serostatus increases virological failure by a 5-fold [53]. The identification of virological failure is possible where viral load measurement is available, which was not routinely done in West Africa. The COHADO cohort is one of the first study to provide viral load data in West-Africa, with measurements more available at the 24th month of follow-up. Viral load access is a real issue in ALHIV care monitoring in Africa, and the prioritization of viral load measurement is universally recommended since 2016 particularly among ALHIV who have high risk of virological failure[53]. In the COHADO clinical sites, the annual viral load measurement is a recent opportunity that should be scaled up and supported in every HIV-care facility, as virological success could be also used to optimize treatment adherence and outcomes of APHIV.

Our study met several limitations. First, we enrolled less than half of APHIV who visited the sites during the inclusion period due to logistical issues, mainly related to health care workers overwork with little time to propose the study and get formally the parent's consent. Although those included did not differ significantly from those not included, the small sample size may have limited the statistical power of our analysis. Second, we selected our APHIV in urban referral center for adolescent HIV care where APHIV are likely receiving better standard of care compared to the general population in these cities. Third, the few time points in the follow-up did not allow us to perform a longitudinal analysis. However, the COHADO cohort reported a small proportion of lost to follow-up reflecting high quality of follow-up in the selected sites. Nevertheless, our study provides original data documenting the feasibility and indirectly the positive effect of accompanying actively the HIV disclosure process using health care worker training on this topic, and routine monitoring of this crucial event. Second, to our knowledge, this study gives a representative and longitudinal assessment of the virological response in APHIV on lifelong ART that could be further used as a reference.

Conclusions

The COHADO cohort study assessed the HIV-disclosure process and outcomes of APHIV in two West African urban clinical sites. Although the frequency of full HIV disclosure remains low, this project encouraged full HIV-disclosure serostatus to APHIV with documented results. The 24-month outcome of APHIV was favorable for slightly less than half of them and differ according to sites.

Urgent interventions are needed to support timely APHIV disclosure practices in both caregivers and health care workers. These interventions to improve full HIV-disclosure to APHIV, may consider disclosure as a dynamic process that should be monitored over time and include caregivers, and healthcare providers. It is also urgent to reduce morbidity and mortality in ALHIV in West Africa. The country effect on the favorable outcomes of ALHIV suggested the need for a better distribution of health workers and resources, the need for context-specific interventions. Finally, it is crucial to monitor closely virological outcomes of ALHIV on lifelong ART. This study provides a reference to tailor context-specific interventions

in West-Africa. Cohort studies among ALHIV such as in pWADA may offer unique opportunity to optimize monitoring and standardized data collection and offer interventional packages to address specific ALHIV issues including disclosure, ART adherence, virological outcome, drug resistance mental and sexual health with the perspective of improving the 90-90-90 cascade in ALHIV population.

Abbreviations

AIDS	Acquired immune deficiency syndrome
ALHIV	Adolescents living with HIV
APHIV	Adolescents living with perinatally-acquired HIV
ART	Antiretroviral therapy
HIV	Human immune deficiency virus
IeDEA	International epidemiologic Database to Evaluate AIDS
IQR	Inter-quartile range
MD	Medical Doctor
NNRTI	Non-nucleoside reverse transcriptase inhibitors
pWADA	pediatric West African Database on AIDS
WHO	World Health Organization

Declarations

Ethics approval and consent to participate

This study received authorizations of the health ministries and national ethics committee of Togo and Côte d'Ivoire. All the participants and their caregivers gave their oral and written informed consent to participate.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

MHDTR. conducted the analyses, wrote the first draft of paper under V.L. supervision.

SD, JJ, DD, KM, EA, JPR and VL reviewed and edited the paper. KM and VL were involved in the database management, the study design, and the statistical analyses. VL was involved in the pediatric leDEA cohort coordination and fund raising. ET, FTE, BB, FB, were in charge of the cohort of adolescents and the database recording in each country involved in the study. All authors have read and approved the final manuscript.

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Tables

Table 1. Characteristic of adolescents included in the COHADO cohort compared to adolescent not included, Abidjan (Côte d'Ivoire), Lomé (Togo), leDEA-pWADA, 2015-2017

	Total (%) N=511	Not included in COHADO (%) N=302	Included in COHADO (%) N=209	P Value
Sex, n (%)				0.61 ⁽¹⁾
Males	239 (46.8)	144 (47.7)	95 (45.4)	
Females	272 (53.2)	158 (52.3)	114 (54.6)	
Age in years, median [IQR]	13 [11-15]	14 [12-16]	13 [11-15]	0.06 ⁽³⁾
WHO clinical stage				<0.01 ⁽²⁾
1,2,3	380 (74.4)	207 (68.5)	173 (82.8)	
4 (AIDS)	43 (8.4)	7 (2.3)	36 (17.2)	
Missing	88 (17.2)	88 (29.4)	0 (0.0)	
CD4, median [IQR]	483 [258-701]	487 [277-678]	534 [278-798]	0.76 ⁽³⁾
Virological suppression, n (%) (Viral load < 50cp/mL)				<0.01 ⁽²⁾
Yes	34 (6.7)	32 (10.6)	2 (1.0)	
No	190 (37.2)	130 (43.0)	60 (28.7)	
Missing	287 (56.1)	140 (46.4)	147 (70.3)	
Site, n (%)				<0.01 ⁽¹⁾
Abidjan (Côte d'Ivoire)	371 (72.6)	263 (87.1)	108 (51.7)	
Lomé (Togo)	140 (27.4)	39 (12.9)	101 (48.3)	
Age initiation ART, median [IQR]	7[4-9]	6[4-9]	7[4-10]	0.12 ⁽³⁾

(1) Chi2 test (2) Fisher's exact test (3) Wilcoxon-Mann-Whitney test

Table 2. Baseline characteristics of the 209 APHIV included in the COHADO cohort, Abidjan (Côte d'Ivoire), Lomé (Togo) leDEA-pWADA, 2015-2017

	Total N=209	(%)	Abidjan, Côte d'Ivoire N=108	(%)	Lomé, Togo N=101	(%)	P-Value ⁽¹⁾
Sex n (%)							0.25
Males	95	(45.4)	45	(41.7)	50	(49.5)	
Females	114	(54.6)	63	(58.3)	51	(50.5)	
HIV disclosure performed, n (%)							<0.01
Yes	87	(41.6)	61	(57.4)	25	(24.8)	
No	122	(58.4)	45	(42.6)	76	(75.2)	
Education level, n (%)							0.01
Primary school	80	(38.3)	31	(28.7)	49	(48.5)	
Middle schools	103	(49.3)	61	(56.5)	42	(41.6)	
High schools	26	(12.4)	16	(14.8)	10	(9.9)	
Residential environment, n (%)							0.91
Urban	187	(89.9)	96	(88.9)	91	(90.1)	
Rural	22	(10.1)	12	(11.1)	10	(9.9)	
Electricity access, n (%)							0.43 ⁽²⁾
Yes	203	(97.1)	106	(98.1)	97	(96.0)	
No	6	(2.9)	2	(1.9)	4	(4.0)	
Piped water access, n (%)							<0.01
Yes	131	(62.7)	101	(93.5)	30	(29.7)	
No	78	(37.3)	7	(6.5)	71	(70.3)	
Living with, n (%)							0.65
Both parents	50	(23.9)	27	(25.0)	23	(22.8)	
Only one parent	93	(44.5)	50	(46.3)	43	(42.6)	
Other family member	66	(31.6)	31	(28.7)	35	(34.6)	
Orphanhood, n (%)							0.03
No	91	(43.5)	44	(40.7)	47	(46.5)	
One parent	91	(43.5)	55	(50.9)	36	(35.6)	
Two parents	27	(13.0)	9	(8.4)	18	(17.8)	
WHO clinical stage, n (%)							<0.01
1,2,3	173	(83.8)	105	(97.2)	68	(67.3)	
4 (AIDS)	36	(17.2)	3	(2.8)	33	(32.7)	
ART regimen, n (%)							0.48
2 NRTI+1NNRTI	168	(81.2)	88	(83.0)	80	(79.2)	
2 NRTI+1PI	39	(18.8)	18	(17.0)	21	(20.8)	
Good ART adherence[†], n (%)							<0.01 ⁽²⁾
Yes	118	(56.4)	57	(52.7)	61	(51.6)	
No	57	(27.3)	24	(22.2)	33	(32.6)	
Missing	34	(16.3)	27	(25.0)	7	(6.9)	
Virological suppression, n/N (%) (Viral load < 50cp/mL)							<0.01
Yes	2/62	(3.2)	0/53	(0.0)	2/9	(22.2)	
No	60/62	(96.8)	53/53	(100.0)	7/9	(77.8)	
CD4 cell count /mm3, median [IQR]	521[281-757]		540[314-753]		484[271.5-760]		0.71 ⁽³⁾
Age in years, median [IQR]	13[11-15]		14[12-15]		12[11-15]		0.01 ⁽³⁾
ART duration in years, median [IQR]	6[4-10]		9[7-11]		5[2-6]		<0.01 ⁽³⁾
Age at ART initiation, median [IQR]	7[4-10]		5[3-8]		9[6-11]		<0.01 ⁽³⁾

(1) Chi2 test; (2) Fisher's exact test; (3) Wilcoxon-Mann-Whitney test †More than 95% of planned doses taken.

Table 3. 24-month outcomes of the 209 APHIV included, by site, in the COHADO cohort, leDEA-pWADA, 2015-2017

	Total N=209	(%)	Abidjan, Côte d'Ivoire N=108	(%)	Lomé, Togo N=101	(%)	P Value ⁽¹⁾
HIV-disclosure performed, n (%)							<0.01
No	54	(25.9)	31	(28.7)	23	(22.8)	
Yes (Since ≤ 2 years)	68	(32.5)	15	(13.9)	53	(52.5)	
Yes (Since > 2 years)	87	(41.6)	62	(57.4)	25	(24.7)	
Follow-up, n (%)							0.18⁽²⁾
Died	6	(2.9)	4	(3.7)	2	(2.0)	
Lost to follow-up	8	(3.8)	3	(2.8)	5	(4.9)	
Transferred out	4	(1.9)	4	(3.7)	0	(0.0)	
Alive & follow-up	191	(91.4)	97	(89.8)	94	(93.1)	
Progression to AIDS WHO stage, n (%)							<0.01⁽²⁾
No	154	(73.7)	91	(84.2)	63	(62.4)	
Yes	7	(3.4)	5	(4.6)	2	(2.0)	
Not applicable	48	(22.9)	11	(11.2)	35	(35.6)	
CD4 count ≥ baseline value (±10%), n (%)							<0.01
No	76	(36.3)	55	(51.4)	21	(21.0)	
Yes	131	(62.7)	52	(48.6)	79	(69.0)	
Missing	2	(1.0)	1	(1.0)	1	(1.0)	
Viral load undetectable (<50 cp/mL)							0.01
No	73	(34.9)	56	(51.8)	17	(16.8)	
Yes	102	(48.8)	49	(45.4)	53	(52.5)	
Missing	34	(16.3)	3	(2.8)	31	(30.7)	
Combined criteria (above), n (%)							0.01
Favorable	94	(45.0)	32	(29.6)	62	(61.4)	
Unfavorable	115	(55.0)	76	(70.4)	39	(38.6)	

(1) Chi2 test (2) Fisher's exact test

†36 already WHO stage 4 at inclusion, 5 Died, 4 Transferred, 1 lost to follow-up, 2 missing

Table 4. 24-month characteristics of the 209 APHIV included according to HIV-serostatus disclosure, in the COHADO cohort, Abidjan (Côte d'Ivoire), Lomé (Togo), leDEA-pWADA, 2015-2017

	Total N=209	(%)	HIV-serostatus disclosed N=155	(%)	HIV-serostatus non disclosed N=54	(%)	P-Value ⁽¹⁾
Sex, n (%)							0.86
Males	95	(45.4)	71	(45.8)	24	(44.4)	
Females	114	(54.6)	84	(54.2)	30	(55.6)	
Site, n (%)							0.34
Abidjan (Côte-d'Ivoire)	108	(51.7)	77	(49.7)	31	(57.4)	
Lomé (Togo)	101	(48.3)	78	(50.3)	23	(42.6)	
Orphanhood, n (%)							0.32
No	91	(43.5)	63	(40.7)	28	(46.5)	
One parent	91	(43.5)	70	(50.9)	21	(35.6)	
Two parents	27	(13.0)	22	(8.4)	5	(17.8)	
WHO clinical stage, n (%)							0.32 ⁽²⁾
1,2,3	164	(78.5)	118	(76.1)	46	(85.2)	
4 (AIDS)	43	(20.6)	35	(22.6)	8	(14.8)	
Missing	2	(0.9)	2	(1.3)	0	(0.0)	
Virological suppression (n=175), (Viral load < 50cp/mL)							<0.24
Yes	102	(58.3)	73	(55.7)	29	(65.9)	
No	73	(41.7)	58	(44.3)	15	(34.1)	
CD4 cell count /mm3, median [IQR]							0.04 ⁽³⁾
	523[353-785]		508[348-750]		596[455-871]		
Age in years, median [IQR]							<0.01 ⁽³⁾
	15[13-17]		16[14-18]		13[12-14]		

(1) Chi2 test; (2) Fisher's exact test; (3) Wilcoxon-Mann-Whitney test

Table 5. Characteristics of HIV-disclosure process to the 155 APHIV disclosed by last contact, by site in the COHADO cohort, leDEA-pWADA, 2015-2017

	Total N=155	(%)	Abidjan, Côte d'Ivoire N=77	(%)	Lomé, Togo N=78	(%)
Person involved in disclosure, n (%)						
Mother	41	(28.1)	30	(43.5)	11	(14.3)
Father	22	(15.6)	18	(26.1)	4	(5.2)
Doctors	8	(5.5)	6	(8.7)	2	(2.6)
Psychologist	84	(56.7)	25	(36.2)	59	(76.6)
Counsellor	3	(2.1)	0	(0.0)	3	(2.1)
Other (Family or association members)	3	(2.1)	0	(0.0)	3	(2.1)
Disclosure performed before ART initiation						
Yes	13	(8.4)	6	(7.8)	7	(8.4)
No	133	(85.8)	64	(83.1)	69	(88.5)
Unknown	9	(5.8)	7	(9.1)	2	(2.6)

Table 6. Correlates of favourable combined 24-month outcome of the 209 APHIV included, in the COHADO, leDEA-pWADA, 2015-2017

	Univariate analysis								Multivariate analysis				
	Unfavorable n=115 (%)		Favourable n=94 (%)		OR (95% CI)		p value	Initial model			Final model		
								aOR (95% CI)	p value		aOR (95% CI)	p value	
HIV-Disclosure					0.79 (0.56-1.11)	0.17			0.45			0.35	
No	27 (23.5)		27 (28.7)		1.00 ---	---		1.00			1.00 -	-	
Yes (Since ≤ 2 years)	35 (30.4)		33 (35.1)		0.94 (0.46-1.92)	0.87		0.48 (0.20-1.16)	0.10		0.50 (0.21-1.15)	0.10	
Yes (Since > 2 years)	53 (46.1)		34 (36.2)		0.64 (0.32-1.27)	0.20		0.67 (0.24-1.82)	0.43		0.65 (0.25-1.72)	0.39	
Site													
Abidjan, Côte-d'Ivoire	76 (66.1)		32 (34.1)		1.00 ---	---		1.00			1.00 -	-	
Lomé, Togo	39 (33.9)		62 (65.9)		3.77 (2.12-6.71)	<0.01		5.11 (1.93-13.5)	0.01		4.41 (2.29-8.50)	<0.01	
Sex													
Males	48 (41.7)		47 (50.0)		1.00 ---	---		1.00			1.00 -	-	
Females	67 (58.3)		47 (50.0)		0.71 (0.41-1.23)	0.23		0.79 (0.43-1.46)	0.46		0.76 (0.42-1.36)	0.35	
Education level					0.89 (0.58-1.33)	0.57							
Primary school	41 (35.6)		39 (41.5)		1.00 ---	---							
Middle schools	60 (52.2)		43 (45.7)		0.75 (0.41-1.35)	0.34							
High schools	14 (12.2)		12 (12.8)		0.90 (0.37-2.18)	0.81							
Piped water access													
Yes	81 (70.4)		50 (53.2)		1.00 ---	---		1.00					
No	34 (29.6)		44 (46.8)		2.09 (1.18-3.70)	0.01		0.82 (0.43-1.98)	0.67				
Electricity access, n (%)													
No	3 (2.6)		3 (3.2)		1.00 ---	---							
Yes	112 (97.4)		91 (96.8)		1.23 (0.24-6.24)	0.80							
Residential environment													
Urban	100 (86.9)		87 (92.6)		1.00 ---	---		1.00					
Rural	15 (13.1)		7 (7.4)		0.53 (0.21-1.37)	0.19		0.52 (0.18-1.44)	0.21				
living with					0.77 (0.53-1.12)	0.17							
Both parents	25 (21.7)		25 (26.6)		1.00 ---	---		1.00					
Only one parent	49 (42.6)		44 (46.8)		0.89 (0.45-1.78)	0.75		1.24 (0.50-3.11)	0.63				
Other family member	41 (35.7)		25 (26.6)		0.60 (0.28-1.28)	0.19		0.77 (0.24-2.45)	0.66				
Orphanhood					0.70 (0.47-1.06)	0.09							
No	42 (36.5)		49 (52.1)		1.00 ---	---		1.00					
One parent	58 (50.4)		33 (35.1)		0.48 (0.26-0.88)	0.01		0.57 (0.24-1.35)	0.20				
Two parents	15 (13.1)		12 (12.8)		0.68 (0.28-1.62)	0.39		0.69 (0.19-2.44)	0.57				
Baseline WHO clinical stage													

1,2,3	101	(87.8)	72	(76.6)	1.00	----	----	1.00					
4	14	(12.2)	22	(23.4)	2.20	(1.05-4.59)	0.03	1.02	(0.42-2.49)	0.95			
Baseline age in years	13	[11-15]	13	[11-15]	0.96	(0.86-1.07)	0.54	1.03	(0.87-1.22)	0.66	1.03	(0.88-1.20)	0.64
Baseline CD4 cells/mm³	540	[265-806]	484	[299-751]	0.99	(0.99-1.00)	0.41	0.99	(0.99-1.00)	0.37			

Figures

Figure 1

Flow chart of inclusion of 209 APHIV in the COHADO Cohort, leDEA-pWADA, 2015.