24-month clinical, immune-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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Research article

Keywords: Adolescents, HIV, disclosure, retention, West-Africa

Posted Date: June 22nd, 2020

DOI: https://doi.org/10.21203/rs.2.15733/v3

Abstract

Background: Adolescents living with perinatally-acquired HIV (APHIV) face challenges including the disclosure of their HIV-serostatus that we explored in the West-African COHADO cohort. We assessed the 24-month outcomes 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. An unfavorable outcome was defined when either death, loss to follow-up, progression to WHO-AIDS stage, a decrease of CD4 count >10% compared to baseline, or a detectable viral load (>50copies/mL) were notified at 24 months. None of these events defined a favorable outcome. We investigated correlates of APHIV favorable 24-month outcome using a logistic regression model.

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]); 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 (± 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 baseline variables, it was not significantly associated with HIV-disclosure but significantly higher for APHIV living in Lomé compared to those in Abidjan (aOR: 17.24, 95%CI [3.69-80.44]).

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.

Background

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 and 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, adolescents 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 growing-up. In many West African pediatric sites, even if children or adolescents are on ART, healthcare providers and caregivers delay HIV-disclosure because of cultural factors and lack of national guidance [21]. Also, caregivers are not ready, and fear the process will lead to disclosing a 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 occurred 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 (IeDEA) pediatric cohort Collaboration, was launched in 2015 in two sites of the West-African IeDEA pediatric cohort in Lomé (Togo) and Abidjan (Côte d'Ivoire). This study is aimed to better document the HIV-disclosure frequency and process over 24 months of follow-up; and to assess the association of HIV-disclosure with the 24-month favorable health outcomes among APHIV since their inclusion in the COHADO cohort.

Methods

Study design

The IeDEA pediatric West African Database to evaluate AIDS (pWADA) is an international multicentric prospective cohort as part of the IeDEA 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 includes children and adolescent living with HIV from 11 pediatric clinical centers in seven West African countries (Benin, Burkina Faso, Côte d'Ivoire, Ghana, Mali, Senegal and Togo) and is 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 APHIV 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 documented 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 IeDEA pediatric central database.

HIV-disclosure process data (disclosure status, date of full disclosure, if delivered over the cohort period, 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.

First, we have compared eligible APHIV included to those not included in the study, and have described APHIV baseline characteristics using median values with inter-quartile ranges (IQR) for continuous variables and proportions for categorized variable, overall and by site. Full HIV-disclosure was assessed at baseline then over the 24 months of follow-up: APHIV were classified at 24-month either as not-HIV disclosed, disclosed to during the past 2 years (after inclusion in COHADO), or disclosed to >2 years, before inclusion in COHADO (in this group, the timing of disclosure was often not recorded). We have compared the baseline characteristics of APHIV according their HIV-disclosure status at 24-month for those unaware of their HIV-status at inclusion in an univariate and an adjusted regression model. Person involved in HIV-disclosure and timing of HIV-disclosure regarding ART initiation were described. Among those who have not been disclosed to at baseline, we described reasons for non-disclosure.

Second, we described the 24-month single and combined outcome components, HIV-disclosure status overall, and according to site. Our endpoint, a 24-month outcome was measured at the 24-month visit combining multiple criteria: (i) vital status (alive, died, lost to follow-up); (ii) WHO AIDS stage progression [35] from baseline; (iii) immunological criteria (% of CD4 cell count difference since baseline); (iv) virological criteria (HIV viral load measured). 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 at data base closing.

After describing each criterion separately, we assessed a combined outcome pooling all criteria at 24 months. An unfavorable combined outcome at 24-month was defined when either death, loss to follow-up, progression to AIDS clinical stage during the study period, a CD4 count decrease >10% compared to baseline or a detectable viral load >50 copies/mL were notified. APHIV with missing data in one of the evaluation criterion were classified using the other criteria. A 24-month favorable combined outcome was defined when none of the above outcomes was notified.

Third, correlates of 24-month favorable combined outcome in COHADO were investigated using a univariate then an adjusted logistic regression analysis, HIV-disclosure being the main explicative variable. We included also all the relevant independent baseline co-variables: age, sex and social factors (access to electricity or piped drinking water, educational level, family environment, etc). We tested for country-specific practices adding an interaction between HIV-disclosure and country. We performed sensitivity analysis regarding clinical and virological missing data, with missing as failures. Model fit was check graphically.

All analyses were performed using STATA 14.2 (Statacorp, College Station, TX, USA).

Results

Selection and inclusion of APHIV in the COHADO cohort

From January 2015 to November 2015, 511 APHIV 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. This was significantly more frequently observed in Abidjan compared to Lomé (Table 1). 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, at inclusion, there significantly more high rates of missing data for WHO AIDS clinical staging and viral load among those not included compared to those included (Table 1).

Baseline characteristics

Baseline characteristics are presented in Table 2. Among the 209 APHIV included, 108 (52%) lived in Abidjan. Overall, 114 (55%) were females; median age was 13 [IQR: 11-15] years, APHIV were significantly older in Abidjan compared to Lomé (p=0.01). Median ART duration prior to inclusion in COHADO was 6 years [IQR: 4-10] and it was significantly longer in Abidjan (9, IQR: [7-11]) compared to Lomé (5, IQR: [2-6]) (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 WHO AIDS stage 4 at baseline, this proportion was significantly 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% with virological suppression (<50 cp/mL).

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

HIV-disclosure characteristics and process

Among the 209 APHIV enrolled, 122 (58.4%) were not informed of their HIV-status at inclusion in COHADO while they were aged of 12 years in median. Questioned about the reason of non-disclosure at baseline, parents/legal guardians of these 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%).

At 24-month endpoint, 87 (41.6%) APHIV were informed of their HIV-status before inclusion, 68 (32.6%) were informed during the follow-up and 54 (25.8%) were still not aware. Baseline characteristics breakdown according to HIV-disclosure status endpoint is presented in Table 3. Overall, 74.2% were fully HIV-disclosed at endpoint (+78.1% compared to baseline, p<0.01).

Among the 122 not informed at inclusion, APHIV disclosed to their HIV serostatus tended to have less CD4 cell count than those not HIV-disclosed (p=0.08). (Table 3). Compared with APHIV not disclosed to their HIV-serostatus, APHIV disclosed during COHADO were significantly older (13 years IQR[11-14] vs 11 years IQR[10-12], p<0.01), with a shorter ART duration (5 years IQR[2-8] vs 7 years IQR[5-9], p=0.03) and more often from Lomé (78% vs 43%, p>0.01). Adjusted on sex, education level, residential environment, person whom APHIV live and baseline clinical AIDS stage, CD4 cell count, age and ART duration, APHIV from Lomé were significantly more likely to be HIV-disclosed during COHADO (adjusted odds ratio (aOR):15.2, 95%CI [3.12-73.9]) (Table 4).

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; doctors were involved in the process for only 5.2% of APHIV (Table 5).

24-month health outcomes

By 24 months, six APHIV had died (2.9%) and eight were lost to follow-up (3.8%). 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 6). Among the 209 APHIV, the 24-month combined health outcome was favorable for 45% of APHIV. This proportion was higher in Lomé (61.4%) compared to Abidjan (29.6%, p<0.01) (Table 6).

The table 7 presents the correlates of a 24-month favorable combined health outcome in APHIV. In univariate analysis, we found that APHIV from Lomé (vs Abidjan), without access to piped water (vs with access to piped water) are significantly more likely to have a favorable outcome.

In multivariate analysis adjusted for all baseline variables, APHIV HIV-disclosure status was not associated with having a favorable 24-month outcome compared to those not disclosed to (Disclosed ≤ 2 years since baseline: aOR=0.29, 95%CI [0.04-1.74], p=0.18; Disclosed >2 years since baseline: aOR=1.06, 95%CI [0.33-3.38], p=0.92) (Table 7). However, APHIV from Lomé were more likely to have a favorable 24-month outcome compared to those from Abidjan (aOR: 17.24, 95%CI [3.69-80.44]). In addition, the interaction between HIV disclosure and site was significant. APHIV disclosed before COHADO in Lomé were less likely to have a favorable 24-month outcome compare to those disclosed before COHADO in Abidjan (aOR:0.12, 95%CI [0.02-0.69]). We performed sensitivity analysis excluding APHIV already AIDS WHO at inclusion, the result remained similar, with no significant effect of HIV-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 IeDEA 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 74.2% 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 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, in adjusted analysis, a favorable outcome was significantly associated with the site: APHIV from Lomé significantly increased the odds of a favorable 24-month outcome compared to those from Abidjan, but no significant association with HIV-disclosure.

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 74.2% 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 Lome where the proportion of APHIV disclosed had increased from 24.8% to 77.2%. One of our hypothesis is that this 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 IeDEA-pWADA sites [44]. This workshop may have changed the health care workers' perceptions and practices regarding HIV-disclosure and explain the significant increase of HIV-disclosure rate at the endpoint, but we also acknowledge that this is can be also 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 programs, 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 HIV-disclosure and fear stigmatization. For many parents, their 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 also found that APHIV HIV-disclosed to tended to have worse clinical and immunological conditions 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 conditions of the patient that prompt their HIV-disclosure to improve urgently their health outcome via the improvement of their adherence to ART. We feel, in regards to the context of our study and factors correlated to HIV-disclosure, that this second hypothesis is most likely. This indication bias could have reduced the HIV-disclosure effect measured after 24 months, since APHIV disclosed have worse clinical and immunological conditions. Similarly, we noted the cohort effect: those disclosed to were significantly older, and therefore were most likely to be at a more advanced stage of the disease progression. 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 relative lower rate could be explained by the shorter follow-up duration.

Overall, 45% of APHIV had a favorable combined 24-month outcome that is rather sub-optimal in terms of quality of ART response. A favorable outcome was not associated to HIV-disclosure but 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 delivery. 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 during COHADO 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 our observation. Because the disclosure data collection was not standardized, nor we did not have the date of disclosure for all APHIV, with a substantial proportion of

APHIV already HIV-disclosed before the inclusion in COHADO cohort and without HIV-disclosure date. So, the association between HIV-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 not disclosed of their 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 study is one of the first cohort to provide viral load data in West-Africa, with measurements substantially more available after 24 months 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 for 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 an indicator used to encourage treatment adherence and therefore outcomes of APHIV. At the contrary, identifying early enough virological failure would be helpful in reinforcing more closely the treatment adherence to re-suppress viral load in these vulnerable population.

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 and relatively short follow-up may have limited the statistical power of our analysis. This flaw could have overshadowed the link between the 24-month health outcomes in APHIV, and several variables such as age, sex or other relevant variables. 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 for instance. 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.

The COHADO study contributes to a better understanding of the disclosure process among APHIV. Since the disclosure of APHIV serostatus is a crucial step in their care, the process should be initiated early

enough and not only for those APHIV at an advanced stage of the disease. HIV-disclosure should be addressed as a dynamic process involving health workers and parents or legal guardian as stakeholder. Overall, the findings of the COHADO study highlight the insufficient response to the current treatment strategies. There is an urgent need to improve treatment adherence and viral response in Abidjan and Lomé, or in others West African cities. Our results should guide the HIV programs to optimize ALHIV quality of care.

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 specifics 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.

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

Funding

Research reported in this publication was supported by the US National Institutes of Health (NIAID, NICHD, NCI and NIMH) under Award Number U01AI069919 (PI: Dabis).

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 IeDEA 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.

Acknowledgments

The authors thank all the participating children and their families, as well as all the members of the hospital teams of the sites involved in the IeDEA West Africa pediatric cohort.

Research reported in this publication was supported by the US National Institutes of Health (NIAID, NICHD, NCI and NIMH) under Award Number U01AI069919 (PI: Dabis). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. J.J. and S.D. were funded by Sidaction.

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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

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Tables

Table 1. Characteristic of eligible adolescents living with perinatally-acquired HIV (APHIV) included in the COHADO cohort compared to those not included, during the inclusion period in Abidjan (Côte d'Ivoire), Lomé (Togo), IeDEA-pWADA, 2015-2017

	Total N=511	(%)	Not included in COHADO N=302	(%)	Included in COHADO N=209	(%)	P Value
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)	
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)
Age initiation ART, median [IQR]	7[4-9]		6[4-9]		7[4-10]		0.12 (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)	
Virological suppression at last, 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)	
CD4, median [IQR]	483 [258-701]		487 [277-678]		534 [278-798]		0.76 (3)

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

	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 drinking 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 at inclusion 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. ART: Antiretroviral therapy

Table 2. Baseline characteristics of the 209 adolescents living with perinatally-acquired HIV included in the COHADO cohort according to sites, Abidjan (Côte d'Ivoire), Lomé (Togo) IeDEA-pWADA, 2015-2017

Table 3. Baseline characteristics of the 209 APHIV included according to HIV-serostatus disclosure at 24-month, in the COHADO cohort, Abidjan (Côte d'Ivoire), Lomé (Togo), IeDEA-pWADA, 2015-2017

	Total N=209		HIV-status disclosed before inclusion in COHADO N=87		HIV-status disclosed during follow-up in COHADO N=68		HIV-status still not disclosed at the last follow-up N=54		P-Value[1]
(%)									0.64
Males	95	(45.4)	37	(42.5)	34	(50.0)	24	(44.4)	
Females	114	(54.6)	50	(57.5)	34	(50.0)	30	(55.6)	
Site, n (%)									<0.01
Abidjan (Côte-d'Ivoire)	108	(51.7)	62	(71.3)	15	(22.1)	31	(57.4)	
Lomé (Togo)	101	(48.3)	25	(28.7)	53	(77.9)	23	(42.6)	
Age at baseline in years, median [IQR]	13[11-15]		15[14-17]		12[11-14]		11[10-12]		<0.01[3]
Orphanhood, n (%)									0.36
No	91	(43.5)	31	(35.6)	31	(47.1)	28	(51.6)	
One parent	91	(43.5)	43	(49.4)	27	(39.7)	21	(38.9)	
Two parents	27	(13.0)	13	(14.9)	9	(13.2)	5	(9.3)	
Education level									<0.01[2]
Primary school	80	(38.3)	14	(16.1)	31	(45.6)	35	(64.8)	
Middle schools	103	(49.3)	49	(56.3)	35	(51.5)	19	(35.2)	
High schools	26	(12.4)	24	(27.6)	2	(2.9)	0	(0.0)	
Piped drinking water access									<0.01
Yes	131	(62.7)	67	(77.0)	32	(47.1)	32	(59.3)	
No	78	(37.3)	20	(22.9)	36	(52.9)	22	(40.7)	
Electricity access, n (%)									0.76
No	6	(2.9)	3	(3.4)	1	(1.5)	2	(3.7)	
Yes	203	(97.1)	84	(96.6)	67	(98.5)	52	(96.3)	
Residential environment									0.53
Urban	187	(89.5)	77	(88.5)	63	(92.6)	47	(87.1)	
Rural	22	(10.5)	10	(11.5)	5	(7.4)	7	(12.9)	
Living with									0.94
Both parents	50	(23.9)	19	(21.8)	18	(26.5)	13	(24.1)	
Only one parent	93	(44.5)	38	(43.7)	30	(44.1)	25	(46.3)	
Other family member	66	(31.6)	30	(34.5)	20	(29.4)	16	(29.6)	
WHO clinical stage, n (%)									0.41[2]
1,2,3	173	(82.8)	73	(83.9)	53	(77.9)	47	(87.1)	
4 (AIDS)	36	(17.2)	14	(16.1)	15	(22.1)	7	(12.9)	
Virological suppression (n=62), (Viral load < 50cp/mL)									0.68[2]
Yes	2	(3.2)	1	(2.9)	0	(0.0)	1	(6.3)	
No	60	(97.8)	34	(97.1)	11	(100.0)	15	(93.7)	
CD4 cell count /mm3, median [IQR]	521[281-758]		492[225 734]		507[262 850]		548[416-843]		0.08[3]

(1) Chi2 test; (2) Fisher's exact test; (3) Kruskal-wallis test

Table 4. Correlates of HIV-disclosure at 24-month among the 122 APHIV not disclosed at inclusion, in the COHADO cohort, Abidjan (Côte d'Ivoire), Lomé (Togo), IeDEA-pWADA, 2015-2017

	Univariate analysis							Multivariate analysis		
			HIV-status disclosed		HIV-status not disclosed			Full model		
	Total N=122	(%)	N=68	(%)	N=54	(%)	P-Value[1]	aOR	(95% CI)	p value
Sex, n (%)							0.54			
Males	58	(47.5)	34	(50.0)	24	(44.4)		1.00	---	---
Females	64	(52.5)	34	(50.0)	30	(55.6)		1.02	(0.41-2.51)	0.96
Site, n (%)							<0.01			
Abidjan (Côte-d'Ivoire)	46	(37.7)	15	(22.1)	31	(57.4)		1.00	---	---
Lomé (Togo)	76	(62.3)	53	(77.9)	23	(42.6)		15.2	(3.12-73.9)	<0.01
Orphanhood, n (%)							0.76			
No	60	(49.2)	32	(47.1)	28	(46.5)				
One parent	48	(39.3)	27	(39.7)	21	(35.6)				
Two parents	14	(11.5)	9	(13.2)	5	(17.8)				
Education level							0.05			
Primary school	66	(54.1)	31	(45.6)	35	(64.8)		1.00	---	---
Middle schools	54	(44.3)	35	(51.5)	19	(35.2)		1.42	(0.49-4.16)	0.51
High schools	2	(1.6)	2	(2.9)	0	(0.0)		1	---	---
Piped drinking water access							0.18			
Yes	64	(52.4)	32	(47.1)	32	(59.3)		1.00	---	
No	58	(47.5)	36	(52.9)	22	(40.7)		0.51	(0.11-2.12)	0.35
Electricity access, n (%)							0.58			
Yes	119	(97.5)	67	(98.5)	52	(96.3)				
No	3	(2.46)	1	(1.5)	2	(3.7)				
Residential environment							0.36			
Urban	110	(90.2)	63	(92.6)	47	(87.1)		1.00	---	---
Rural	12	(9.8)	5	(7.4)	7	(12.9)		0.62	(0.11-3.27)	0.58
Living with							0.95			0.93
Both parents	31	(25.4)	18	(26.5)	13	(24.1)		1.00	---	---
Only one parent	55	(45.1)	30	(44.1)	25	(46.3)		1.17	(0.37-3.67)	0.78
Other family member	36	(29.5)	20	(29.4)	16	(29.6)		0.99	(0.27-3.61)	0.98
WHO clinical stage, n (%)							0.19[2)]			
1,2,3	100	(81.9)	53	(77.9)	47	(87.1)		1.00	---	---
4 (AIDS)	22	(18.1)	15	(22.1)	7	(12.9)		0.44	(0.10-1.84)	0.26
CD4 cell count /mm3, median [IQR]										
	546[305-843]		508[262-850]		548[416-843]		0.19 [3]	0.99	(0.99-1.00)	0.88
Virological suppression (n=27), (Viral load < 50cp/mL)							1.00			
Yes	1	(3.7)	0	(0.0)	1	(6.3)				
No	26	(96.3)	11	(100.0)	15	(93.7)				

Age at inclusion in years, median [IQR]						
12[11-13]	13[11-14]	11[10-12]	<0.01[3]	1.86	(1.31-2.63)	<0.01
Age at ART initiation, median [IQR]						
6[4-9]	8[4-11]	5[3-7]	<0.01[3]			
ART duration in years, median [IQR]						
6[3-9]	5[2-8]	7[5-9]	0.03[3]	0.96	(0.80-1.15)	0.69

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

Table 5. Characteristics of the HIV-disclosure modalities to the 155 adolescents living with perinatally-acquired HIV disclosed at 24 months by sites in the COHADO cohort, IeDEA-pWADA, 2015-2017

	Total N=155	(%)	Abidjan, Côte d'Ivoire N=77	(%)	Lomé, Togo N=78	(%)
Person involved in HIV disclosure, n (%)						
Mother	41	(26.5)	30	(43.5)	11	(14.3)
Father	22	(14.2)	18	(26.1)	4	(5.2)
Doctors	8	(5.2)	6	(8.7)	2	(2.6)
Psychologist	84	(54.2)	25	(36.2)	59	(76.6)
Counsellor	3	(1.9)	0	(0.0)	3	(2.1)
Other (Family or association members)	3	(1.9)	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. 24-month component and combined outcomes of the 209 adolescents living with perinatally-acquired HIV included, by sites in the COHADO cohort, IeDEA-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	(22.7)	
Yes (Since ≤ 2 years)	68	(32.5)	15	(13.9)	53	(52.5)	
Yes (Since > 2 years)	87	(41.6)	62	(57.4)	25	(24.8)	
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 during the study period, n (%)							**<0.01[2]**
Yes	7	(3.3)	5	(4.6)	2	(2.0)	
No	154	(73.7)	91	(84.2)	63	(62.4)	
Already AIDS WHO at inclusion	36	(17.3)	3	(2.8)	33	(32.7)	
Died, LTFU, transferred out, missing	12	(5.7)	9	(8.3)	3	(2.9)	
CD4 count decrease ≥ baseline value (±10%), n (%)							**<0.01**
Yes	76	(36.3)	55	(51.4)	21	(21.0)	
No	131	(62.7)	52	(48.6)	79	(69.0)	
Missing	2	(1.0)	1	(1.0)	1	(1.0)	
Viral load detectable at 24-month (>50 cp/mL)							**0.01**
Yes	73	(34.9)	56	(51.8)	17	(16.8)	
No	102	(48.8)	49	(45.4)	53	(52.5)	
Missing	34	(16.3)	3	(2.8)	31	(30.7)	
Combined outcome † , n (%)							**<0.01**
Unfavorable	115	(55.0)	76	(70.4)	39	(38.6)	
Favorable	94	(45.0)	32	(29.6)	62	(61.4)	

[1] Chi2 test [2] Fisher's exact test

†Unfavorable combined outcome at 24-month: death or progression to AIDS during the study period or CD4 count decrease >10% compared to baseline or detectable viral load.
Favorable outcome: none of the outcomes defined above notified.

Table 7. Correlates of favorable combined 24-month health outcome (definition table 5) of the 209 APHIV included, in the COHADO, IeDEA-pWADA, 2015-2017

	Univariate analysis							Adjusted analysis		
	Unfavorable combined outcome n=115 (%)		Favorable combined outcome n=94 (%)		OR	(95% CI)	p value	Full model aOR		p value
HIV-Disclosure					0.79	(0.56-1.11)	0.17			0.29
No	27	(23.5)	27	(28.7)	1.00	---	---	1.00	---	---
Yes (Since ≤ 2 years)	35	(30.4)	33	(35.1)	0.94	(0.46-1.92)	0.87	0.29	(0.04-1.74)	0.18
Yes (Since > 2 years)	53	(46.1)	34	(36.2)	0.64	(0.32-1.27)	0.20	1.06	(0.33-3.38)	0.92
Site										
Abidjan, Côte-d'Ivoire	76	(66.1)	32	(34.1)	1.00	---	---	1.00	---	---
Lomé, Togo	39	(33.9)	62	(65.9)	3.77	(2.12-6.71)	<0.01	**17.24**	**(3.69-80.44)**	**<0.01**
HIV Disclosure*Site (Interaction)							<0.01			0.02
HIV disclosed ≤2years_Lomé					0.67	(0.08-5.36)	0.70	0.92	(0.10-7.99)	0.94
HIV disclosed >2years_Lomé					0.12	(0.02-0.63)	0.01	**0.12**	**(0.02-0.70)**	**0.02**
Sex										
Males	48	(41.7)	47	(50.0)	1.00	---	---	1.00	---	---
Females	67	(58.3)	47	(50.0)	0.71	(0.41-1.23)	0.23	0.773	(0.39-1.38)	0.33
Education level							0.63			0.88
Primary school	41	(35.6)	39	(41.5)	1.00	---	---	1.00	---	---
Middle schools	60	(52.2)	43	(45.7)	0.75	(0.41-1;35)	0.34	0.85	(0.39-1.83)	0.68
High schools	14	(12.2)	12	(12.8)	0.90	(0.37-2.18)	0.81	1.02	(0.29-3.57)	0.96
Piped drinking 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	0.59	(0.23-1.52)	0.28
Electricity access, n (%)										
Yes	112	(97.4)	91	(96.8)	1.00	---	---	1.00	---	---
No	3	(2.6)	3	(3.2)	1.23	(0.24-6.24)	0.80	1.45	(0.22-9.70)	0.69
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	0.60	(0.21-1.71)	0.34
Living with							0.35			0.22
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	0.99	(0.43-2.25)	0.98

	Other family member	41 (35.7)	25 (26.6)	0.60	(0.28-1.28)	0.19	0.54	(0.23-1.30)	0.17
Age at inclusion, median [IQR]	13 [11-15]	13[11-15]	0.96	(0.86-1.07)	0.54	1.09	(0.91-1.30)	0.31
ART duration in years, median [IQR]	8[4-10]	6[4-8]	0.90	(0.83-0.97)	0.01	0.98	(0.89-1.09)	0.78

OR: Odds Ratio; aOR:adjusted Odds Ratio

Figures

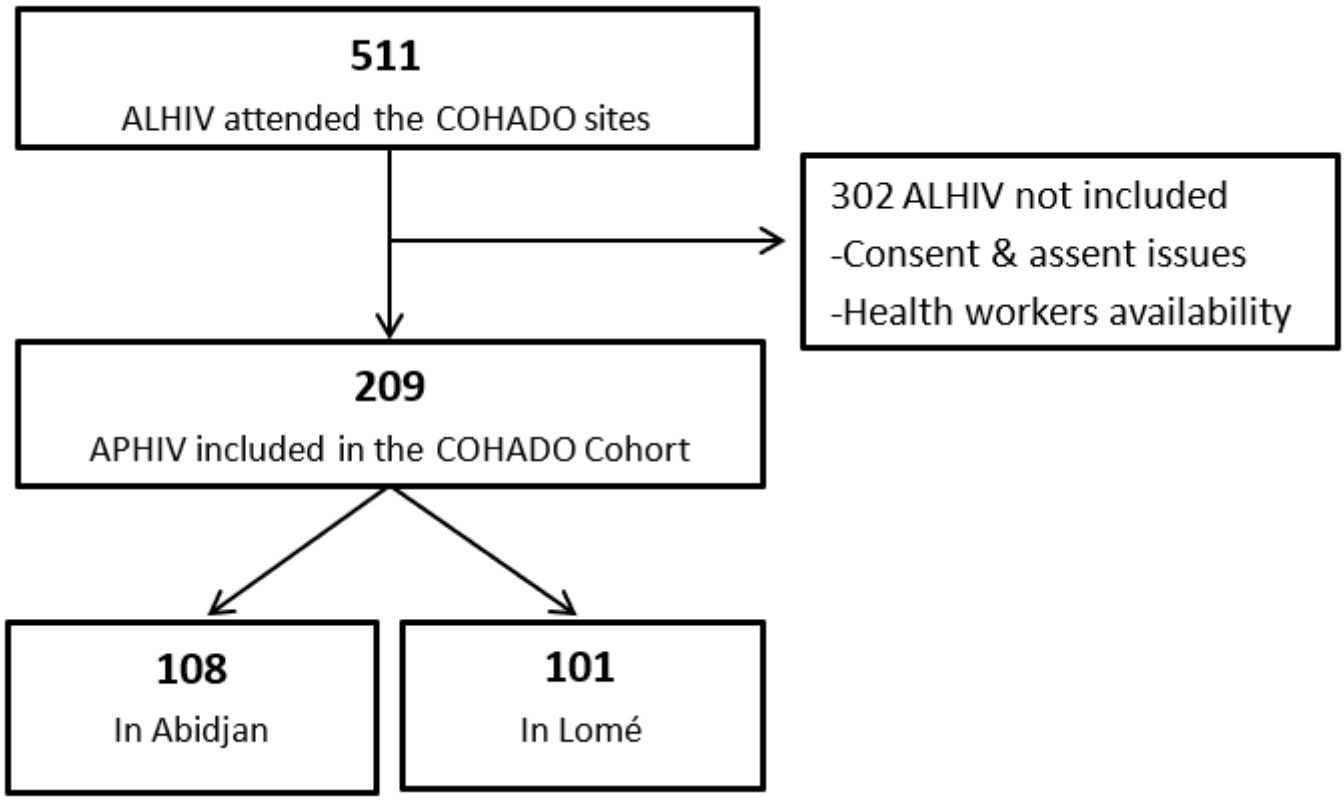

Figure 1

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