

## ORIGINAL ARTICLE

## CLINICAL OUTCOMES OF ADOLESCENTS LIVING WITH HIV AFTER TRANSFER TO ADULT CARE IN A TERTIARY HOSPITAL, ETHIOPIA: A RETROSPECTIVE OBSERVATIONAL STUDY

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### ABSTRACT

**Introduction:** Transferring adolescents living with HIV to adult care is beyond changing the services location. The transition process will significantly affect the success of antiretroviral therapy (ART) for individual patients and the overall HIV program in a country. This study assessed the clinical outcomes of adolescents living with HIV who were transferred to adult care in Addis Ababa, Ethiopia.

**Methods:** A facility-based retrospective observational study was conducted at a tertiary care hospital. Data collection was based on a review of the clinical records of adolescents living with HIV that were transferred from pediatric to adult ART clinic. Data was extracted from paper-based and electronic medical records of patients seen from January 2016 to December 31, 2017, using a structured data extraction tool. The data were analyzed using SPSS version 24.

**Result:** Out of the 151 adolescents included in this study, 18 (11.9%) were lost to follow up (LTFU) after one year of transfer to adult care. There was one death, which occurred three months after the transfer. At the time of transfer, 11 (7.4%) of the adolescents had fair or poor adherence to treatment recommendations, and after six months of the transfer, this number increased to 52 (34.7%). In addition, the percentages of adolescents with CD4 count < 200 cells/mm<sup>3</sup> increased from 2.6% at the time of transfer to 6.7% six months after transfer. This represented a statistically significant decrease in the mean CD4 count of 50 (13.3 vs 86.9,  $p=0.008$ ).

**Conclusions:** Although the majority of adolescents remained engaged in their follow-up after transfer to adult care, there was a significant gap in adherence to their treatment. These are also reflected by a subsequent increment of adolescents with a CD4 count of less than 200 cells/μl. Thus, more should be done to ease the adolescents' transition process and improve their adherence.

**Keywords:** Adolescents, Antiretroviral, HIV, Transition, Lost to follow up

### INTRODUCTION

Adolescents living with HIV (ALHIV) are enrolled in HIV care, mostly in pediatric clinical settings. When they grow into adulthood, they need to be transferred from pediatric to adult care. Healthcare transition (HCT) does not merely change location from pediatrics to adult clinics; instead, it is a planned and purposeful transition of adolescents to engage them in their health and disease management meaningfully (1). The success of the transition process significantly affects the success of antiretroviral treatment (ART) for individual patients as well as for the overall HIV program in a country (2). However, this transition can be difficult due to potential barriers.

HCT from pediatrics to adult care is challenging for several reasons. For example, fear of disrupting the relationship between the patient and the health care provider in pediatric care emphasizes the need for youth-friendly services (1-4).

The presence of HIV makes this process more complicated due to associated psychosocial and developmental problems and comorbidities in the context of coping with a chronic, potentially stigmatizing disease (3,4). Adolescents and young adults living with HIV are also highly vulnerable to depression (4,5). In addition, they may deny their HIV status (6) and are prone to risk-taking (7), which may lead them to higher risks of HIV transmission, treatment interruption, adherence problems, treatment failure, and loss to follow-up (2). These issues may be more pertinent for prenatally infected adolescents compared to behaviorally infected adolescents (8).

ART has been successful in reducing mortality among people living with HIV/AIDS (PLWHA). However, improvements among adolescents and young adults have been less pronounced than among children and adults (9).

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Results from retrospective cohort studies in North America have shown that poor adherence and loss to follow-up (LTFU) are common after transfer to adult care (10,11). Although CD4 count  $>500$  cells/mm<sup>3</sup> (10) and retention rates (11) were initially high, these declined significantly by the second year after transition. Both samples were small and done in resource-rich countries, where population characteristics and health systems are different from those found in Low and Middle-Income Countries (LMIC). A study with a large sample from Kenya was also consistent with these findings, demonstrating higher LTFU among youth than other age groups (12). Our study focused on assessing the clinical outcomes of adolescents living with HIV after the transition to adult services in TASH, where there are no specialist services for adolescents (13). Findings will have the potential to inform the development of appropriate services for this age group in this setting and other similar settings in LMIC.

## METHODS

### *Setting*

Tikur Anbessa Specialized Hospital (TASH), where this study was conducted, is the largest teaching hospital in Ethiopia, with over 700 beds, and offers diagnosis and treatment to over 400,000 patients a year. Pediatric Infectious Diseases Clinic (PIDC) gives comprehensive care and treatment for over 300 children per month. It is staffed with one consultant specialist on pediatric infectious diseases, one fellow in pediatric infectious diseases, one to two residents, one general practitioner (GP), and five nurses. Adult ART clinic is a separate clinic that evaluates over 3000 adults per month and has no separate clinic for adolescents at the time of the study. It is staffed with two consultant specialists on infectious diseases, one to three residents, and eight nurses. Both PIDC and adult ART clinics give service five days per week during office hours and half days during weekends.

### *The transition process*

TASH pediatric patients with HIV are followed in the PIDC and transferred to adult ART clinics when they reach at least 16 years of age, or whenever the staff thinks they are ready to be transferred. The adult ART clinic is found in the same compound, and patients get transferred along with their complete paper-based medical follow-up chart, and follow-up would continue with the same medical follow-up chart at the adult ART clinic. At the time of the study, there was no separate transition service or adolescent clinic with its guideline in the hospital to facilitate care transfer.

### *Study design and period*

An institution-based retrospective observational study was conducted in adolescents living with HIV transferred into adult ART clinics from January 2016 to December 31, 2017.

### *Sample size determination*

The sample size calculated using the single population proportion formula,  $n = Z^2 * P * (1-P) / d^2$  and adjusted sample size  $(n) = (N * n) / (N + n)$ , where  $Z = 1.96$  for 95% confidence interval,  $P = 24\%$ , taken from another study reporting lost to follow up rate (10), and “d” is the desired precision (0.05). N is the finite population estimated to be 330 at the time of data collection. The adjusted final sample size was found to be 151.

### *Study population and sampling*

Clinical records were reviewed to identify adolescents living with HIV transferred from PIDC to adult ART clinics. The study population was all adolescents who were attending adult clinics and fulfilling the inclusion criteria (those engaged in care in pediatric care before the transfer, and elapsed time of at least one year since the transfer) were included. Adolescents living with HIV who were directly linked to the adult ART clinics (has not been in pediatric clinic), and elapsed time of less than one year since transfer were excluded.

### *Study variables*

The primary outcome variables were LTFU, adherence to their current drug regimen, immunological response, treatment failure, and mortality.

### *Definitions*

#### *Age groups:*

In this study, the definitions used for adolescents (age 10-19 years) and youth (10-24 years) were similar to those used in the literature (14)

The formal transition of adolescents living with HIV was defined as the “purposeful, planned movement of adolescents with chronic physical and medical conditions from child-centered to adult-oriented health care systems” (15)

#### *Functional status is defined as:*

1. Working: If they can perform everyday work in and out of the house.
2. Ambulatory: If they can perform activities for daily living.
3. Bedridden: Individuals not able to perform activities of daily living.

**Lost to follow up (LTFU):** Has not visited health care or follow up for more than six months (15,16).

**Engaged in care:** Visited health care on their appointment within the past three to six months (15, 16).

**Good adherence:** If they took more than 95% of their medication or missed <2 doses per month.

**Fair adherence:** If they took 85-94% of their medication or missed 3-5 doses per month.

**Poor Adherence:** If they took less than 85% of their medication or missed >5 doses per month.

**Treatment failure:** After six months of treatment if there is one or all of the following (15, 16).

1. New or recurrent clinical events indicating severe immunodeficiency.
2. CD4 count falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm<sup>3</sup>.
3. Plasma viral load above 1000 copies/ml.

#### **Data collection**

The data extraction form was adopted from the ART intake form, follow-up form, and after reviewing similar literature (10,11). The checklist was prepared in English and had four parts. It contained socio-demographic questions, clinical data, adherence to the ART, and clinical outcomes. Data were abstracted at different time points; at the start of ART, at transfer, six months post-transfer, one year post-transfer. Two nurses collected the data after one day of training on the structured checklist and collection techniques.

The principal investigator supervised the data collecting process.

#### **Data analysis**

Data were cleaned before entry. Then it was coded and entered into SPSS version 24 for analysis and descriptive statistics. Descriptive statics (proportion, percentage, ratio, frequency distribution, central tendency, and measure of dispersion) and tabular presentation were used to summarize the data. Paired-t-test was used to compare pre-and post-transition CD4 count.

#### **Ethical considerations**

Ethical clearance was obtained from the Department Research and Publication Committee (DRPC) of the Department of Pediatrics and Child Health, College of Health Sciences, Addis Ababa University. No personal identifier information was included in the study.

#### **RESULTS**

One hundred fifty-one adolescents were transferred from PIDC to adult ART clinics during the study period. Out of the 151 adolescents, 87 (57.6%) were male. The median (interquartile range [IQR]) duration of stay at PIDC was 10 (IQR 9, 11) years. The median age at diagnosis of HIV was 8 (IQR 7, 10) years and the median age at transfer was 18 (IQR 17, 19) years. The median age at the time of data collection was 20 (IQR 19, 21) years, with the median duration of stay at adult ART clinic follow-up was two years (IQR 2, 2)(Table 1).

**Table 1:** Socio-demographic Characteristics of Adolescents Living with HIV in 2016/2017 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

<b>Variable</b>	<b>n (%) or median (IQR)</b>
<b>Gender</b>	
Male	87 (57.6)
Female	64 (42.4)
Age at diagnosis	8 (7.10)
<b>Age at start of ART</b>	
Less than 18 months	1 (0.7)
18 to 59 months	1(0.7)
60 months to 120 months	114 (75.5)
Above 120 months	35 (23.2)
Age at transfer to adult clinic	18 (17.19)
Current age	20 (19.21)
Age at disclosure	12 (11, 14)
Duration of stay at pediatric	10 (9.11)
Duration of stay at adult care	2 (2, 2)

One hundred thirty-two (87.4%) remained engaged in care after one year of transfer to adult care. Eighteen (11.9%) were lost from follow-up (LTFU); two of them were LTFU within six months of transfer and 16 within one year of transfer. One death occurred three months after the transfer, and the cause of death was respiratory failure secondary to ARDS.

#### **Adherence**

Eleven (7.4%) of the adolescents had fair or poor adherence at the time of transfer, and six months post-transfer, this number has increased to 52(34.7%). At one year of transfer, the rate of poor or fair adherence was 33(22.0%), slightly lower than six months post-transfer.

#### **Medical outcomes**

At the time of transfer, 73(48.3%) adolescents had a CD4 count above 500 cells/ $\mu$ l, 50(33.1%) between 200 cells/ $\mu$ l and 500 cells/ $\mu$ l, only 4(2.6%) were

having severe immune-compromised with a CD4 count below 200 cells/ $\mu$ l, and the rest 24(15.9%) patients had unknown CD4 count. This changed at six months of post-transfer, with an increase in the proportion of adolescents with CD4 count < 200 cells/ $\mu$ l was 10(6.7%). This represented a statistically significant decrease in the mean CD4 count of 50 (13.3 vs86.9,  $p=0.008$ ). A one-year post-transfer CD4 count was done only for 13 adolescents, making it challenging to analyze. Viral load was done only for a few patients, so there was inadequate data to make comparisons. ART regimen changed to 24(15.9%) adolescents post-transfer, of whom 18 were due to treatment failure. There was no difference in WHO clinical staging, functional status, and weight pre and post-transfer (Table 2).

**Table 2:** Pre and post-transition Outcomes of Adolescents Living with HIV in 2016/2017 at Tikur Anbessa Specialized Hospital, Addis Ababa

Variables	At start of	At transfer	At 6month of	At 1 year of
	ART		transfer	transfer
	n (%)	n (%)	n (%)	n (%)
<b>WHO clinical stage</b>				
Stage I	5 (3.3)	144 (95.4)	143 (95.3)	142 (94.7)
Stages II,III, IV	146 (96.7)	7(4.6)	7(4.7)	8(5.3)
<b>CD4 (cells/mm<sup>3</sup>)</b>				
Below 200	51 (33.8)	4 (2.6)	10 (6.7)	0(0)
>200	91 (60.2)	123(81.5)	65 (43.3)	13(8.7)
Unknown	9(6.0)	24(15.9)	75(49.7)	137(91.3)
<b>Viral load copies/<math>\mu</math>l</b>				
Undetectable	0(0)	6 (4.0)	14 (9.3)	11 (7.3)
Detectable	0(0)	42(27.8)	14(9.3)	23(15.3)
Unknown	151(6.6)	103(68.2)	122(81.4)	116(77.4)
<b>Functional status</b>				
Working	79 (52.3)	129 (85.4)	145(96.7)	143 (95.3)
Ambulatory	68(45.0)	1(0.1)	0(0)	0(0)
Unknown	4(2.6)	21(13.9)	5(3.3)	7(4.7)
<b>Adherence</b>				
Good	148 (98)	140 (91.6)	98 (65.3)	117(78.0)
Fair or Poor	3(0.2)	11(7.4)	52(34.7)	33 (22.0)

## DISCUSSION

This study reported that 18 adolescents living with HIV were lost to follow-up after one year of transfer to adult care from a cohort of 151 (11.9%). Although the expectation from adult clinics receiving these adolescents was assuming responsibility for their care tasks, the result of this study showed that they were not prepared for it at the time of transition. This was shown by an increasing proportion of adolescents with poor adherence, reflected by a drop in their CD4 counts, which raised concern in their post-transition care.

The lost follow-up in this study was consistent with findings from Quebec, Canada (10), Atlanta, Georgia (11) and the Netherlands (17). This lost to follow-up could be due to lack of preparation for the transfer and/or difficulty adapting to the new place and health workers. Adolescents may fear being with adults and/or may think they lose their confidentiality (18). Different follow-up styles between pediatric and adult follow-up clinics may lead to adaptation problems (10). Another study also identified a lack of communication between adult and pediatric clinics and low developmental readiness barriers for successful transition (19). In addition, the age by itself may pose difficulty in shouldering responsibility for their care and follow-up. It is known that adolescents are different from adults in many aspects and need special attention. Adolescent services are believed to bridge pediatric and adult provision of care by delivering age-appropriate communication and physical environments (20). However, the overburdened adult OPDs in TASH setting may not be suitable to offer special attention and follow-up.

At the time of the transfer, 11(7.4%) of adolescents had fair or poor adherence, and six months and one-year post-transfer, this number has increased to 53 (35.1%), 34 (22.5), respectively. Routine CD4 and viral load are laboratory markers to monitor the success of ART. Viral load monitoring was not done for most adolescents, making it difficult to compare; significantly higher number of adolescents had CD4 count below 200 cells/ $\mu$ l at six months of post-transfer.

With regards to post-transfer mortality, there was one death (0.7%) in a year period, which was comparable to the mortality rate among transitioned adolescents in the United Kingdom, which was 0.9 % (21) but much lower than the mortality rate of transitioned adolescents in Canada, which was 8.8% (9).

Although, the adherence problem was lower than the report from Quebec, Canada (10), it was an issue of concern because it is far lower than the UNAIDS target (90% adherence) (22), and coupled with a decrement of CD4. This could also be due to age-related risk-taking behavioral changes seen in adolescents, like discontinuing medication, requiring age-specific adherence counseling and follow-up.

### *Limitations*

The study clearly showed the challenges associated with transfer of care of adolescents living with HIV from pediatric to adult HIV; however, it has several limitations including the retrospective observational study design, adherence was documented using self-report which is subjected to recall bias, and it was not possible to confidently evaluate the predictors of the adverse outcomes observed.

### *Conclusions*

Although most adolescents remained engaged in their follow-up post-transfer to adult care, there was a significant gap in adherence, and significantly higher number of adolescents had a CD4 count of less than 200 cells/ $\mu$ l and treatment failure six months and one year post-transfer. So we strongly recommend developing a guideline for all health care facilities that give HIV care on preparing and transferring adolescents to adult HIV care. In addition, training adolescents on self-care and medication adherence before the transfer, some period of follow up on both pediatric and adult clinics before the transfer, and maintaining the relationship with the peers in the pediatric side are recommended as possible solutions to ease transfer. Further prospective research is needed on this issue to generate more comprehensive and authoritative evidence.

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***Conflict of interests:*** We declare that we have no competing interests.

### *Authors' contributions*

AG and WA conceived and designed the study. All authors (AG, WAmo, WA) prepared the study proposal, participated in data collection, and have analyzed the data. AG drafted the manuscript. WA actively involved in the data interpretation and critically reviewed the manuscript. All authors (AG, WAmo, WA) have read and approved the final manuscript.

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