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Modelling adverse treatment outcomes of HIV-infected adolescents attending public-sector HIV clinics in Lusaka

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ABSTRACT

Background: In resource-limited setting, there is scarce evidence comparing antiretroviral therapy (ART) outcomes among HIV-infected adolescents to that of other age groups.

Methods and study design: We analysed data from 25 ART facilities in Lusaka District, comparing treatment-naïve ART-eligible young adolescents (10–14 years), older adolescents (15–19) and young adults (20–24 years) initiating first-line ART to those aged 24 years or older. The adjusted relative risk (RR) of failure to achieve an adequate CD4 response (defined as failure to increase CD4 count by $\geq$ 50 cells/mm^3 at 6 months or by $\geq$ 100 cells/mm^3) at 6 or 12 months after ART initiation was modelled using log-binomial regression. The effect of age group on mortality and loss to follow-up (LTFUP; $\geq$60 days since scheduled visit date) was estimated using adjusted Cox proportional hazards models, respectively. This was a routine retrospective design using program data.

Results: Of the 94,023 patients initiating ART from May 2004 to February 2011, 1303 (1.4%) were young adolescents, 1440 (1.5%) were older adolescents and 5825 (6.2%) were young adults. 85,455 (90.9%) were 24 years or older at the time of ART initiation. Compared with adults, both young adolescents (RR: 0.88, 95% confidence interval [CI]: 0.76–1.01 at 6 months and RR: 0.80, 95% CI: 0.69–0.93 at 12 months) and older adolescents (RR: 0.82, 95% CI: 0.71–0.95 at 6 months) were less likely to achieve adequate CD4 response. No evidence of a difference in mortality risk was observed among older adolescents (hazard ratio [HR] 1.20, 95% CI: 0.93–1.56) compared with adults; however, there was a reduced risk of mortality in young adolescents compared with adults (HR: 0.61, 95% CI: 0.40–0.92). Young adolescents were less likely to be LTFUP following ART initiation (HR: 0.74, 95% CI: 0.59–0.92), while older adolescents and young adults were reported to be more likely to drop out of care (HR: 1.54 95% CI: 1.33–1.78; HR: 1.51 95% CI: 1.40–1.63 respectively).

Conclusion: Older adolescents and young adults had poorer ART treatment outcomes, including failure to achieve adequate CD4 recovery and failure to remain in long-term care, when compared with adults. Interventions are necessary to help increase outcomes and retention in care.

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Introduction

According to the WHO, the number of adolescents on antiretroviral therapy (ART) continues to escalate.[1] This reveals major developments in access to ART and effective treatment of perinatally infected children but also newly acquired HIV infections through high-risk behaviour during early adolescence.

An increasing number of adolescents are entering care in adult-oriented HIV facilities, but there are few criteria in place to guide the clinic staff in how best to medically take care of adolescents and young adults within these settings. Few studies in the region have even investigated the outcomes of ART in the evolving group of HIV-infected adolescents and compared them with the adult group.[1,2]

There is sufficient evidence alluding that the adult-oriented HIV model for care have not met the needs of adolescents and young adults as they face unique challenges in the management of HIV.[3] Studies from the USA have suggested that HIV-positive adolescents and young adults in adult-oriented HIV facilities are not likely to start treatment, not likely to achieve viral suppression and not likely to stay on treatment compared with HIV-infected adults.[3,4] Other studies conducted in Sub-Saharan Africa have also shown that substantial proportions of children and adolescents are being initiated into treatment with advanced disease and comorbidities that tend to be associated with early mortality and poor treatment outcomes.[5,6]

In resource-limited settings, there is little evidence comparing ART outcomes among HIV-infected adolescents to that of other age groups. Few studies that have been done using programmatic data have reported that despite improved and highly successful programmatic coverage with ART, significant numbers of adolescent and adults drop out of care at various points along the treatment pathway and, therefore, treatment improvements fail to reach adequate numbers of children and adolescents.[7–12] This phenomenon has resulted in not understanding how and why adolescents and young adults drop out of treatment programs, especially that retention of people on ART and ensuring adherence to treatment are critical determinants of successful long-term treatment outcomes. It is also important to establish reasons why there is a discrepancy between the adolescent and adults dropout rates which in turn have compromised treatment outcomes. This study, therefore, aims to compare the treatment outcomes of HIV-infected adolescents attending public-sector HIV clinics in Lusaka to HIV-infected adults.

Methods

We conducted a retrospective analysis of data from 25 ART facilities in Lusaka District using SmartCare data base. SmartCare is an electronic health record system (EHR) which was developed in 2004 and deployed by the Ministry of Health Zambia, in collaboration with the Centers for Disease Control and Prevention (CDC), Zambia, and many other implementing partners. It is used in providing and keeping information on continued care for people living with HIV.

The analysis compared treatment-naïve ART-eligible young adolescents (10–14 yrs), older adolescents (15–19 yrs) and young adults (20–24 yrs) with those aged 24 years and older.

Age categories were defined according to the World Health Organization (WHO).[4] Adjusted relative risk estimates of failure to achieve adequate CD4 response is defined as the failure to increase CD4 count by 50 cells/mm^3 at 6 months or by 100 cells/mm^3 at 12 months. Estimates were obtained using log-binomial regression.

The effect of age group on mortality and loss to follow-up (LTFUP, 60 days since the last scheduled visit date), was estimated using adjusted Weibull and Cox proportional hazards models, respectively. For descriptive statistics, the median (interquartile range [IQR]) for continuous values or proportions (categorical values) was calculated and Kruskal–Wallis or Chi-squared test was used for comparisons. Data were analysed using Stata/MP version 14.1 (Stata Corporation, Texas, TX, USA).

Study outcomes

(1) Immunological and virological responses

We evaluated the failure to attain an adequate CD4 count response (defined as the failure to increase CD4 count by $\geq$ 50 cells/mm^3 at 6 or 12 months after ART initiation),[7,8] while the change in CD4 count during the course of therapy was calculated by deducting the CD4 count at 6 or 12 months from the baseline CD4 count, which was presented as the IQR at each time point.

Virological failure was defined as two or more consecutive HIV–RNA viral loads of $\geq$400 copies/ml following suppression below this level. Never achieving an RNA-PCR viral load of <400 copies/ml or a detectable HIV viral load ($\geq$400 copies/ml) at 6 months or 12 months after ART initiation was defined as the failure to achieve virologic suppression.[7–9]

(2) Mortality and loss to follow-up

All-cause mortality was abstracted from patients' programmatic data base of the Ministry of Health supported by the Ministry of Health in Zambia. Record from the data base was verified using National Registration cards (NRCs). Loss to follow-up and mortality was defined as having missed an appointment with the doctor (clinical assessment, antiretroviral drug pick up or counsellor visit) by $\geq$ 3 months after the planned visit date. LTFUP and mortality were assessed at three points: (i) ever – any time during follow-up; (ii) during the first 12 months after ART initiation or (iii) after the first 12 months. For the death or LTFUP, person–time accrued from ART initiation until the earliest of death, LTFUP. The time on ART (in months) was calculated from ART initiation until the earliest of LTFUP, death, transfer out or close of dataset.

(3) Pre-ART clinical screening

Clinical screening was done following WHO staging criteria.[4]