HIV Infection Presenting in Older Children and Adolescents: A Case Series from Harare, Zimbabwe

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Background. Symptomatic human immunodeficiency virus (HIV) infection during late childhood and adolescence may be an emerging problem in southern Africa, but it is one that is poorly described. We investigated social and clinical features in patients of this age group presenting to a HIV treatment clinic with special adolescent services in Harare, Zimbabwe.

Methods. All patients aged 8–19 years and their guardians who attended an adolescent HIV treatment clinic were asked to consent to an interview and a review of medical notes.

Results. Of 32 patients, 17 (53%) were male. The median CD4 cell count at presentation was 101 cells/μL (interquartile range, 35–197 cells/μL). Sixty-two percent experienced stunting (mean Z score for height-for-age, -2.55; 95% CI, -2.00 to -3.10), and all presented with World Health Organization stage 3 or 4 HIV infection. The median age at the first HIV test was 11 years, with a median of 3.5 years delay since the first HIV-related illness. Recurrent respiratory tract infections, skin complaints, diarrhea, and past tuberculosis were the most common HIV-related complaints. Seventeen patients (55%) were double orphans, and 10 (62%) surviving parents were known to be HIV positive.

Conclusions. In this small study, HIV-infected adolescents were profoundly immunosuppressed, with characteristics suggesting long-standing HIV infection. The equal sex distribution and high incidence of parental and sibling mortality were consistent; the majority of children had HIV-infected parents and, therefore, were potentially long-term survivors of HIV infection due to mother-to-child transmission. Greater recognition of the substantial burden of undiagnosed HIV infection and acquired immunodeficiency syndrome in this age group is needed, together with services aimed at reducing barriers to earlier diagnosis and initiation of treatment.

Southern Africa has experienced by far the most severe HIV epidemic of any global region, with extremely high prevalence among antenatal clinic attendees [1]. Although scale-up of interventions to prevent mother-to-child transmission is a regional priority, these interventions still reach only a minority of mothers [1].

The natural history of survival with untreated HIV infection during infancy is dominated by high risk of rapid HIV progression, with a survival probability of only 45% by the age of 2 years in African cohorts [2, 3]. Although natural history beyond 5 years is poorly characterized, recent cohort data have challenged the long-held assumption that survival to adolescence is exceptional and instead suggest that $\leqslant$10% of HIV-infected infants will reach adolescence in the absence of treatment for HIV infection [4]. In support of this, recent population-based surveys in the region have found a higher-than-expected HIV prevalence among older children (5–9 years) of 4%–7% [5–8]. Follow-up to the most recent South African study found HIV infection to be equally distributed between boys and girls and essentially restricted to children of HIV-positive mothers, making vertical transmission the most likely source [1].

Adolescents, especially young women, are also at high risk of sexual acquisition of new HIV infection and

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have been the focus of considerable HIV prevention efforts [9]. The need for treatment for HIV infection, however, has not been prioritized for this age group, except in the context of a future need for children growing up while receiving antiretroviral therapy (ART). Health care providers may be reluctant to diagnose HIV infection, given the devastating implications for the family, and HIV testing services for persons aged <16 years tend to be more expensive and less available than adult services, because they are accessible only through referral to hospital clinics [10, 11].

In Zimbabwe, the prevalence of HIV infection among antenatal clinic attendees was ⩾30% nationally during the last half of the 1990s—and has only recently begun to decrease [12, 13]—exposing infants born during that period to a ⩾10% risk of becoming infected with HIV. Local physicians report that the emergence of symptomatic HIV infection first presenting during late childhood or early adolescence as the HIV epidemic matured reflected long-term survival from mother-to-child transmission in the majority of cases (J. Hakim, J. Matenga, A. Reid, M. Dixon; personal communication).

In response, a dedicated adolescent HIV treatment clinic was started by a nongovernmental clinic in Harare, Zimbabwe, to provide diagnostic counselling, HIV testing, and antiretroviral treatment. The aim of the current study is to describe the clinical features and social circumstances of all patients aged 8–19 years who attended this clinic.

METHODS

Patient recruitment. During a 5-month period, the outpatient records of all patients attending the Connaught Clinic in Harare, Zimbabwe, were screened; patients aged 8–19 years and their guardians were asked for written informed consent to participate. Connaught Clinic is a nongovernmental health care clinic that provides counselling, testing, and means-tested free or subsidized treatment for HIV infection, including ART. Preference was given to patients from 2 low-income suburbs of Harare. Approximately 350 patients in total were registered at the clinic.

Data collection. A standard questionnaire was administered to the patient and/or guardian. This included questions about social circumstances, family history, and events leading up to the diagnosis of HIV infection. Clinical history included illnesses and treatment before and after diagnosis of HIV infection. Patient-held records were screened for primary and secondary health care visits, diagnoses made, and details of investigations and treatment of HIV infection and tuberculosis. Clinical examination included height, weight, and World Health Organization staging [14]. Date of birth was taken from a national identity card, birth certificate, or vaccination card. During initial investigations, complete blood cell count, plasma glucose level, and CD4+ T lymphocyte count (CD4 cell count) were obtained, and liver function tests were performed.

Data was entered into an access database and analyzed using EpiInfo, version 6.0 (Centers for Disease Control and Prevention). Mean Z scores for height- and weight-for-age were calculated using growth reference curves developed by the National Centre for Health Statistics and the US Centers for Disease Control and Prevention with data from the Fels Research Institute and US Health Examination surveys [15]. These growth curves are recommended by the World Health Organization for international use [16]. Scores that were 2 SDs below the mean of the normal distribution for height- and weight-for-age were considered to represent stunting and being underweight, respectively [15]. Weight-for-height scores were not calculated, because reference curves extend up to the age of 13 only [15].

Ethical considerations. All participants and their guardians gave written informed consent. Ethical approval was obtained from the Medical Research Council of Zimbabwe.

RESULTS

Thirty-two patients participated, with no refusals. The median age was 12 years (interquartile range [IQR], 11–15 years), and 17 (53%) were male (table 1).

Table 1. Baseline characteristics of HIV-infected patients attending an HIV clinic in Harare, Zimbabwe.

Characteristic	No. (%) of patients
Age, years	
9–11	12 (38)
12–15	14 (44)
16–19	6 (19)
Age at diagnosis, years	
<5	2 (6)
6–9	9 (28)
⩾10	21 (66)
Delay in diagnosis,[a] years	
0–2	13 (46)
3–5	6 (21)
⩾6	9 (32)
Male sex	17 (53)
Orphan status[b]	
Double	17 (55)
Maternal	3 (10)
Paternal	9 (29)
Primary guardian	
Biological parent	11 (34)
Other relative	11 (34)
Orphanage	10 (31)

[a] Interval between first reported HIV-related illness and first HIV test.
[b] Data missing for 1 patient.

Family history and social circumstances. Only 2 participants (6%) had both parents still alive; 12 (39%) had lost 1 parent, 17 (55%) had lost both parents, and data were missing for 1 patient. Only 11 mothers (35%) were still alive. Nine participants lived with their grandmother, aunt, or uncle, and 1 orphan lived with an older sibling. Known causes of death for 23 of the 46 parents who had died were tuberculosis for 9 (20%), AIDS for 11 (24%), malaria for 2 (4%), and trauma for 1 (2%); the cause was not known for the remainder of parents.

Chronic ill health was reported by 7 (44%) of the surviving parents. HIV infection had been diagnosed in 10 (62%) of the surviving parents. Of the participants, 45% were caring for sick parents, guardians, and/or siblings, and 19% reported regularly missing school as a result. Among 26 participants with siblings, 44 of the siblings were living, and 5 were dead; 32 living siblings (73%) were reported to be chronically unwell. Only 9 siblings had been tested for HIV infection, and 4 were HIV positive.

Age at first diagnosis of HIV infection. Twelve participants (38%) had their first HIV test at Connaught Clinic. For 29 participants (91%), HIV testing was indicated because of illness, and only 2 (6%) were tested routinely because of parental HIV infection. The median age at diagnosis was 11 years (IQR, 9–14 years); 65% of the participants were aged ⩾10 years at diagnosis, and only 2 were diagnosed before the age of 5 years. Among the guardians, 75% had suspected that the participant was infected with HIV before testing. The median delay between the first serious illness and diagnosis of HIV infection was 3.5 years (IQR, 1–6 years).

Clinical manifestations. Ninety-seven percent of the participants had below average height-for-age, and 100% were below average weight-for-age. The mean Z score (±SD) for height-for-age was −2.55 ± 1.43 (95% CI, −2.00 to −3.10), and the mean Z score (± SD) for weight-for-age was −2.32 ± 1.01 (95% CI, −1.94 to −2.70). Sixty-three percent and 58% of participants had a Z score for height-for-age and for weight-for-age of less than −2, respectively. All participants had World Health Organization stage 3 or 4 HIV infection at presentation. The median CD4 cell count at diagnosis was 101 cells/μL (IQR, 35–197 cells/μL). The majority of participants (91%) reported recurrent upper respiratory tract infections, chronic skin problems, and/or chronic diarrhea. Tuberculosis had been diagnosed on ⩾1 occasion in 19 participants (59%) before the diagnosis of HIV infection was made; an additional 8 patients (25%) had been treated for tuberculosis at or after diagnosis of HIV infection. The spectrum of illnesses reported before and after diagnosis of HIV infection is shown in table 2.

HIV treatment. Trimethoprim-sulfamethoxazole prophylaxis had been started by 13 participants (41%) before the diagnosis of HIV infection was confirmed. Most participants commencing ART for the first time started with a regimen of 2 nucleoside reverse-transcriptase inhibitors (NRTI) and a non-nucleoside reverse-transcriptase inhibitor (NNRTI). Two participants had previously received ART; 1 had received didanosine and hydroxyurea therapies, followed by 2 NRTIs and 1 NNRTI, and a regimen of 1 NNRTI and 2 NRTIs failed for the other. For both participants, financial constraints affected adherence to the treatment regimens.

DISCUSSION

This study documents the clinical manifestations and family circumstances of symptomatic HIV infection that was diagnosed during late childhood or adolescence among patients attending an HIV treatment clinic for adolescents in Harare, Zimbabwe. Similar to findings from population-based surveillance of HIV infection in this age group in southern Africa, we report an equal sex distribution [6–8, 17] and high burden of parental ill health and mortality [1], which suggests that most of our participants were children of HIV-infected parents. Population-based studies report rates of orphanhood of ⩽35% by the early adolescent years in this region—with a predominance of paternal over maternal orphans [6–8, 18–20]—which is unlike the higher rate of parental deaths reported among our participants who also reported chronic ill health and deaths among siblings. The loss of a mother generally appears to have graver consequences than the loss of a father, with respect to survival, schooling, and welfare [19, 20].

Table 2. Clinical features of HIV-infected older children and adolescents presenting to an HIV clinic in Harare, Zimbabwe.

Variable	No. (%) of patients
Baseline CD4 cell count, cells/μL	
<50	10 (31)
50–200	14 (44)
>200	8 (25)
Z scores	
Weight-for-age less than −2	16 (52)
Height-for-age less than −2	18 (62)
Diagnoses at or preceding HIV test	
Recurrent sinusitis/upper respiratory tract infection	21 (66)
Chronic diarrhea	20 (63)
Tuberculosis	19 (59)
Chronic skin conditions	18 (56)
Oral candidiasis	13 (41)
Shingles	10 (31)
Oesophageal candidiasis	6 (19)
Recurrent pneumonia	5 (16)
Other AIDS-defining diagnoses[a]	7 (22)
Chronic HIV-related conditions[b]	8 (25)

[a] Pneumocystis pneumonia (in 2 patients), cryptococcal meningitis (in 1 patient), and HIV wasting syndrome (in 4 patients).

[b] Cor pulmonale (in 1 patient), bronchiectasis (in 3 patients), sero-negative arthritis (in 1 patient), cardiomyopathy (in 1 patient), recurrent venous thrombosis (in 1 patient), and cardiovascular accident (in 1 patient).

Notable features from the clinical history and examination were a high prevalence of stunting, suggesting long-standing growth failure; a high burden of chronic HIV-related complications that were unlikely to respond to ART [21–23]; and a long delay between the first manifestations of immunosuppression and diagnosis of HIV infection. Growth failure, manifested by stunting, is a prominent feature of HIV infection in children [24–26]. The high prevalence in this series contrasts with low rates of stunting in recent cross-sectional surveillance among children attending primary school in Harare [27]. There was also other evidence of long-standing ill health, with most participants having low median CD4 cell counts at diagnosis and reporting long-standing chronic skin, respiratory, and gastrointestinal symptoms. Over half of the participants had been treated for tuberculosis before diagnosis of HIV infection, and a substantial minority had chronic HIV-related complications, including chronic lung and cardiovascular disease and arthritis.

Delayed diagnosis contributed to the high burden of morbidity in this case series. No free-standing HIV-testing facilities exist in Harare for clients <16 years, and therefore, diagnosis can only be accessed in health care facilities, which is common in other African countries [10, 11]. Most participants reported a substantial delay between their first clinical manifestation of HIV infection and their first HIV test, which suggests that demand and/or supply-side barriers to diagnostic testing exist for this age group. Only 25% of parents or guardians had not suspected HIV infection before diagnosis, and health care providers had clearly considered the diagnosis, because trimethoprim-sulfamethoxazole prophylaxis had been started without HIV testing in 41% of the participants. Low-cost ART has only recently become available in Zimbabwe, and access to pediatric formulations is still very limited, potentially contributing to a sense of futility regarding HIV testing.

There were several limitations to this study. The series was small, and there was likely to have been referral bias towards sicker patients. The majority of participants were referred from the community, with only 2 participants being referred after hospitalization. Clinical histories were obtained retrospectively from participants and their guardians, but the histories were also checked against patient-held hospital and primary clinic records, including tuberculosis treatment cards. Diagnostic facilities in most public health care settings in Harare are limited, and diagnoses are often based on clinical judgement and response to treatment.

To our knowledge, this is the first description of HIV infection presenting among older children and adolescents in a setting in Africa with a high prevalence of HIV infection. We have not investigated the mode of transmission, but the equal sex ratio and high burden of ill health, death, and HIV infection among surviving parents and siblings raise the potential of long-term survival following mother-to-child transmission. Our participants presented with advanced HIV infection after having experienced long delays in diagnosis. Evidence suggesting that this is an emerging clinical problem comes from several sources. Marston et al. [4] used African studies that measured survival of HIV-infected children (direct data) or survival of children of HIV-infected parents (indirect data) to develop a model to project the effects of the HIV epidemic on child mortality. They reported that age-specific mortality decreased after infancy and increased before adolescence. If an assumption is made that HIV infection is the only cause of death, then the model predicted survival to 1 year of age to be 67% and to 5 years of age to be 39%. In addition, the model predicted that 13% of children would survive to 10 years of age. Shisana et al. [9] calculated the prevalence of HIV infection by age among children who were hospitalized or attending primary health care facilities in Free State, South Africa, during 2004. Among children aged 6–9 years, the prevalence of HIV infection was 14.6% (95% CI, 12.7%–16.8%) and was higher among hospitalized children (21.5%) than among those attending primary health care facilities (13.7%). These estimates are from a country with a relatively recent HIV epidemic, and thus, the proportion of admissions that are HIV related is likely to be higher in other countries in the region with more mature epidemics, such as Zimbabwe. Parotitis, otitis media, and upper respiratory tract infection were identified as common presentations among vertically infected ART-naive children aged 6–12 years in Uganda [28]. Of HIV-infected ART-naive children aged 1–14 years recruited to the Children with HIV Prophylaxis Study in Zambia during 2001–2003, 195 (38%) were aged ⩾10 years. Of this cohort, 74% of the children had ⩾1 prior hospitalization; reasons were tuberculosis (32%), pneumonia (26.3%), malnutrition (marasmus, kwashiorkor, both, or unspecified; 11.6%), diarrhea and/or dehydration (10.2%), malaria (9%), nonsevere respiratory tract infection (6.9%), and nonrespiratory severe infection (3.8%) [29].

Greater recognition of the substantial burden of undiagnosed HIV infection in older children and adolescents is needed, and there is a need for more services aimed at the special needs of this unusually vulnerable age group to provide accessible and sympathetic HIV testing and treatment services, appropriate posttest counselling, ongoing psychological support, and drug formulations for low-weight individuals. Further research is needed to better define the burden and unique clinical and social problems that face young people with symptomatic HIV infection if they are to benefit fully from the use of ART in Africa.

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