Reasons for Delay in Initiation of Antiretroviral Therapy in a Population of HIV-Infected South African Children

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Abstract

The aim of this study was to determine the reasons for delay of antiretroviral therapy (ART) in eligible HIV-infected children after the implementation of the South African National ART programme in April 2004, and to describe implemented interventions to improve ART access. This descriptive, retrospective audit included all HIV-infected children attending an ART clinic from April to December 2004, summarizing the following: (i) demographic data; (ii) HIV disease stage; (iii) CD4+ counts/percentages; (iv) ART eligibility and (v) reasons for ART delay. There were 276 study participants with a mean age of 4 years 4 months (range: 1 month–13 years). According to the South African national guidelines, 243 children were eligible for ART, but only 96 children were initiated on treatment during the study period, which was 39.5% of the eligible group and 34.8% of the total group. Important reasons for treatment delay were: (i) co-infection with tuberculosis (26.4%); (ii) lack of human resources (20.3%); (iii) socio-economic obstacles (17.3%) and (iv) incorrect disease stage classification (13.7%). Paediatric ART clinics need to co-operate closely with existing tuberculosis clinics for the effective management of tuberculosis co-infection; address socio-economic factors of HIV-affected families, especially the legal guardianship in orphans and improve their own staff capacity and the education of medical staff in HIV/AIDS management.

Introduction

No age group in South Africa (SA) is untouched by the HIV pandemic. The National Household HIV Prevalence and Risk Survey of SA Children (2004) estimated an HIV prevalence of 6.2% among ages 2–9 years, a daunting proportion that will demand efficient and effective clinical management [1]. The SA HIV epidemic is also superimposed on an existing burden of poverty, aggravated in HIV-affected families by the financial cost of chronic disease, death of adult breadwinners, funeral expenses and orphanhood [2]. Children are particularly vulnerable to effects of poverty and social insecurity, dependent as they are on adult care [3].

Antiretroviral therapy (ART) is associated with a marked reduction in morbidity and mortality, but has been unavailable to most SA patients prior to 2004 [4]. The SA Health Ministry launched the Comprehensive HIV and AIDS Care, Management and Treatment in November 2003, focusing on improving quality and duration of life through social and nutritional intervention, prophylaxis for opportunistic infections, adequate treatment of infectious diseases and ART [5]. ART eligibility criteria for children at programme implementation were: (i) CD4+ percentage <15% in children over 18 months; (ii) CD4+ percentage <20% in children under 18 months; (iii) modified World Health Organization (WHO) Stages 2 or 3 disease in all age groups; (iv) recurrent HIV-related hospital admissions ($\geq$2 admissions/year) or (iv) prolonged (>4 weeks) HIV-related hospital admission [6].

With the high HIV disease burden in children at our site it was decided to determine the factors that delayed initiation of ART and to describe interventions implemented to address these factors to ensure initiation of ART as soon as possible in eligible children.

Patients & Methods

This retrospective, descriptive study was conducted between 1 April and 31 December 2004 at Kalafong Hospital, a large regional state hospital serving a predominantly urban population in the Gauteng Province of SA. All HIV-infected ART-naïve children attending the paediatric ART clinic and whose parents/legal guardians consented to the study were enrolled. The study protocol was approved by the Ethics Review Committee of the Faculty of Health Sciences of the University of Pretoria. Information obtained included: (i) demographic data; (ii) HIV disease stage; (iii) CD4+ counts/percentages; (iv) eligibility for ART and (v) reasons for delay of ART. According to national guidelines, the ART initiation process comprises an initial screening visit, a second confirmation/education visit and a treatment initiation visit [6]. For the study purpose, patients requiring additional visits prior to ART initiation were classified as experiencing delayed or deferred treatment.

Results

There were 276 children enrolled, with a male to female ratio of 1.2:1 and a mean age of 4 years 4 months (range: 1 month–13 years). The majority of children had symptomatic disease, with 83.7% in modified WHO Stages 2 or 3 (qualifying for ART according to SA guidelines [6]) and 83.0% in Stage C according to CDC staging [7] (Table 1).

Table 1 Percentages of children with modified WHO- and CDC clinical disease stage

Staging	Percentage
Modified WHO stage	
Stage 1	16.3%
Stage 2	42.0%
Stage 3	41.7%
CDC clinical stage	
Stage N	3.6%
Stage A	13.4%
Stage B	46.0%
Stage C	37.0%

The mean absolute CD4+ count was 622 cells mm^{-3} (range: 2–4290 cells mm^{-3}), with the mean CD4+ percentage 15.3% (range: 0.2–43.7%) (Fig. 1). Severe immunological suppression (CDC Stage 3) was present in 68.2%, and 57.2% were eligible for ART by national CD4+ percentage criteria.

In total, 243 children (88%) were eligible for ART, while only 96 children began treatment during the study period, which was 39.5% of those eligible and 34.8% of the total group. One or more reason for the delay of ART was present in 157 patients (64.6%), of whom 121 patients (49.8%) had one reason, 32 (13.2%) patients had two and 4 (1.6%) had three reasons.

Reasons for delay in ART initiation are illustrated in Fig. 2. Active or possible tuberculosis co-infection was the primary reason for deferment of ART (26.4%), with 43 children receiving tuberculosis treatment and a strong clinical suspicion of tuberculosis in another nine. To improve patient care at this ART clinic and to speed-up ART initiation, attention was given to improve the

diagnosis of tuberculosis in children by strict adherence to a tuberculosis diagnostic protocol, active follow-up of tuberculosis culture results, the active decision regarding the need for tuberculosis treatment in every patient and a more aggressive approach of treating tuberculosis on clinical suspicion soon after the patient's presentation to the hospital services. Improved co-operation with the tuberculosis services was also promoted on a local level.

Fig 1 CD4+ percentages by age groups.

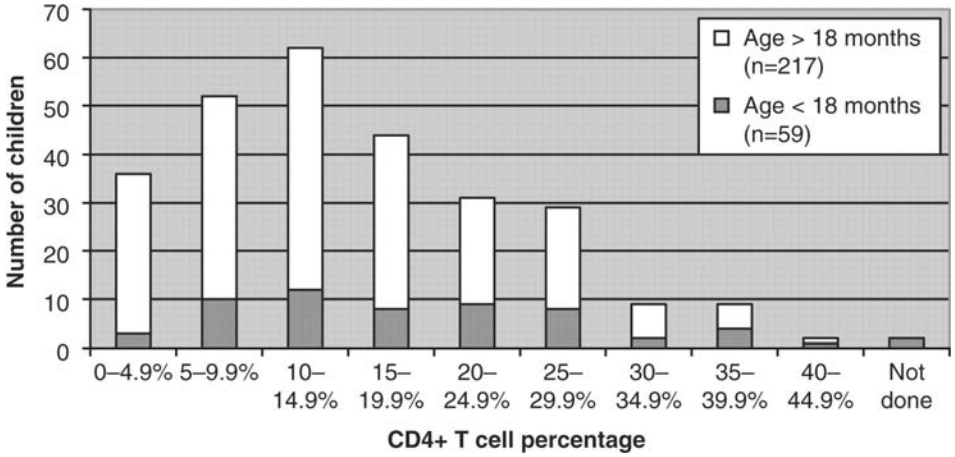
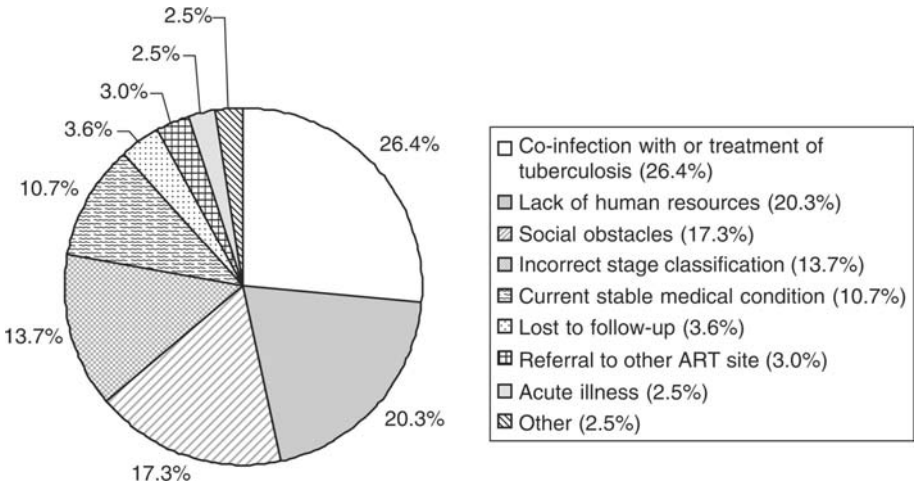


Fig 2. Reasons for delay/deferment of ART.



Insufficient human resources were the next in importance in delay of treatment in eligible children (20.3%). The sudden availability of ART necessitated the treatment implementation in a large number of children with advanced disease (modified WHO Stage 3 and/or very low CD4+ percentages) who were preferentially enrolled. The clinic staff at the time had two paediatricians (with other hospital duties), one intern, two nurses, one counsellor and shared with the adult HIV clinic: one general practitioner, one dietician, one pharmacist and one social worker. There were 58 patient visits to our clinic at initiation of the ART programme in April 2004, which steadily increased monthly to 158 visits in November 2004, which was an increase of 63% (Table 2). An average of 11 children were started on ART/month during the study period.

Interventions implemented were the employment of a dedicated paediatric ART doctor, an additional counsellor, an administrative officer, as well as additional staffing through a NGO, the Foundation for Professional Development, which included a doctor, nursing assistant, administrative officer, social worker and a shared pharmacist. Clinic hours were also expanded.

Data management was enhanced by improvements in the clinic's filing system, as well as the development of a Microsoft Access database at no cost by an independent consultant.

The presence of one or more social problems was the third most important reason for delay of ART (17.3%). These problems included food insecurity, lack of transport, no legal guardian, history of suboptimal adherence to medical treatment, caregiver's refusal to disclose child's status to another adult, denial of the child's status, caregiver's denial of the need for ART, caregiver's ill health and substance abuse. Interventions implemented included the employment of a dedicated paediatric ART social worker, close telephonic patient follow-up for missed appointments and starting of a transport fund financed through public donations. HIV testing and referral of caregivers for necessary care was also prioritized in order to ensure holistic care for the family. Furthermore, with the help of the social workers, expedited legal guardianship was sought and obtained.

Table 2. Number of patient visits and patients initiated on the ART programme/month from April to December 2004

	New patient visits	Follow-up patient visits	Total patient visits	Patients started on ART
April	4	54	58	25
May	2	80	82	7
June	9	85	94	6
July	11	104	115	22
August	16	118	134	7
September	9	113	122	7
October	4	152	156	11
November	4	154	158	6
December	2	69	71	5
Total	61	929	990	96

Incorrect clinical or immunological staging was the fourth most common treatment obstacle (13.7%). Errors included incorrect nutritional assessments (n = 15), an incomplete history of previous medical problems (n = 6) and incorrect diagnosis of concomitant diseases, e.g. disseminated tuberculosis (n = 4). Furthermore, CD4+ values were unavailable in five children at the time of classification. Subsequently all staff members were sent to formal training courses and continual in-house staff training is taking place. A periodic file review is done by a paediatrician to ensure quality of patient care. Regarding the nutritional status assessment, all patients are assessed by the dietician before the physician visit. Furthermore, logistical organization was improved to ensure that patient's laboratory results are obtained prior to clinic visits and are filed in the patient's file.

Twenty-one children (10.7%) had previously been classified with advanced HIV-disease, but when ART became available the children's clinical condition was stable and ART was deferred. Six children (3.0%) were referred to an ART centre closer to home, while another five (2.5%) had acute life-threatening illnesses necessitating emergency treatment. Two children (1%) died at home just prior to ART initiation. Two brothers (1%) of non-SA citizenship were referred to an ART site in their country of origin. One child (0.5%) had severe mental disability and after intensive counselling, the family declined ART.

ART regimens were prescribed according to national guidelines [6], and in 77.1% ART was started at an outpatient visit, while 22.9% started as inpatients during hospitalization for acute illness and/or advanced HIV-disease.

Discussion

In 2003, the World Health Organization estimated that only 2% of HIV-infected Africans were receiving ART, making the continent a global priority for expansion of ART availability. The '3 by 5' initiative, launched later that year, set a target of 3 million patients on ART worldwide by the end of the year 2005 [4]. ART is a rational and cost-effective choice, even in developing countries, and the ability to rapidly scale-up adult ART treatment services has been well documented, including in the SA setting [8, 9]. The WHO '3 by 5' progress report (June 2005) highlighted the urgent need for improved paediatric HIV care, estimating that 660 000 children were in need of ART [10]. Previously cited reasons for the small numbers of children on ART include lack of paediatric fixed dose combinations, unpalatable drug formulations, healthcare workers' inexperience in paediatric ART and inadequate laboratory facilities [11, 12]. In this survey, we found that a large percentage of children assessed were eligible for ART according to the national protocol [6], but that the following reasons resulted in a treatment delay, namely tuberculosis co-infection, poor social circumstances and orphan state, as well as insufficient and inexperienced staff members.

The HIV-epidemic has led to a resurgence of tuberculosis worldwide, which has in turn exacerbated the HIV burden [13]. It is therefore not surprising that tuberculosis co-infection was a major cause for delay in ART in our study population. In HIV-infected children, the difficulty in diagnosing tuberculosis poses major risks to suboptimal patient care, and improved diagnostic tools are urgently needed [13, 14]. The SA ART guidelines advise that tuberculosis treatment should preferably be completed before ART initiation, as long as the patient's clinical condition permits this delay, in order to decrease pill burden and minimize adverse drug reactions [5, 6, 15]. The guidelines further state that patients with advanced HIV-disease should begin ART 2 months after starting tuberculosis treatment, although there is insufficient clinical data to support this, and more research is needed [6]. Close co-operation between ART and tuberculosis services is essential for optimal patient management [16].

Poverty is a key threat to the well being of children in sub-Saharan Africa. Social assistance must be accessible for needy patients, with clear guidelines regarding eligibility and transparency in the granting process [3, 17]. Social support, poverty alleviation and legal guardianship are especially relevant for orphans, since delay in ART is often due to the absence of a legal guardian and inadequate social support structures [3, 17, 18].

The lack of skilled health care workers is a serious concern in many parts of sub-Saharan Africa, exacerbated by the so-called 'brain drain' and loss of life due to the HIV epidemic itself [2, 10, 19]. Eligible children will be missed by clinic staff unless health care workers receive adequate training in paediatric HIV care. Caregivers, especially HIV-positive mothers, also need to receive ART in the context of a holistic, family-centred HIV service. Although ART is an outpatient treatment, it is essential that ART clinics have hospital services available for referral of patients with complex care issues, such as multiple diagnoses, side effects and complications of drugs and complex decision-making regarding ART [5]. Referral to treatment sites closest to the patient's home can either be done before the initiation of treatment, or in the case of sites with less clinical expertise in paediatric ART, as soon as the child's condition has stabilized on treatment. This will ensure that larger ART sites retain capacity to enrol new children, and that more peripheral ART sites build up experience in the treatment of children.

In conclusion, the ART treatment programme for children in SA faces many challenges of which co-infection with tuberculosis, human resource constraints and social problems are the major obstacles to the initiation of ART. These obstacles require a concerted effort by policy makers and clinicians alike to create interventions to overcome them, and the holistic care by a multidisciplinary team is essential. Team members should include both HIV- and tuberculosis clinicians and nurses, trained counsellors who can address the cultural complexities of the disease in affected families and social workers who can address social obstacles in all families in need of assistance, as well as legal guardianship issues in orphans. Also important are dieticians to address the nutritional needs of children, many of whom come from poverty-stricken homes, knowledgeable pharmacists to assist in the complex drug adherence and drug-interaction issues encountered as well as adequate administrative personnel to back-up the large-scale treatment programmes.

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