Research Article

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# HIV Morbidity and Mortality in the Pediatric Population of Côte d'Ivoire

Folquet AM[1,2*], Dainguy ME[1], Kangouté M[1], Kouakou C[1], Kouadio E[1], Zobo Konan N[1], Oka Bérété G[1], Kouadio Yapo G[1], Gro Bi A[1], Djivohessoun A[1], Djoman I[1] and Jaeger FN[3,4,5]

[1]Pediatrics department of Cocody Teaching Hospital, Abidjan, Côte d'Ivoire

[2]Felix Houphouët Boigny University, Abidjan, Côte d'Ivoire

[3]Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Côte d'Ivoire

[4]Swiss Tropical and Public Health Institute, Basel, Switzerland

[5]University of Basel, Basel, Switzerland

*Corresponding author: Folquet AM, Pediatrics department of Cocody Teaching Hospital, Abidjan, 25 BP 567 Abidjan 25, Côte d'Ivoire, Tel: 00 225 07 84 83 17; E-mail: amorissanifolquet@hotmail.fr

## Abstract

**Introduction:** The aim of our study was to describe the morbidity and mortality patterns in HIV-positive pediatric patients followed at the unit in charge of Pediatric HIV, in the pediatrics department of Cocody University Teaching Hospital (CHU-Cocody).

**Method:** This hospital-based retrospective study focused on 218 pediatric patients enrolled at the CHU-Cocody from November 28th 2005 until June 30th 2010. Outcomes of children with anti-retroviral therapy (group A) and children without (Group B) anti-retroviral therapy were described and compared. Antiretroviral Therapy (ART) - eligibility followed national guidelines thus withholding treatment for immune-competent children or those with contraindications to ARTs such as increased transaminases (>10x) or vital distress.

**Results:** The average age of children in group A, was 66.11 months, they were symptomatic in 84.74% of cases, and presented with severe immunodeficiency in 54.74%. The children in group B were younger (mean age=49.14 months), mostly only mildly symptomatic (39.80%) and thus usually without severe immunodeficiency (64.29%). Nearly all children were infected with HIV-1 and receiving cotrimoxazole prophylaxis. There were 764 disease events that occurred during follow-up including 633 in group A and 131 in group B. Anemia (p=0.036) and pneumonia (p=0.011) were more frequent in group A. Hospitalizations were more common in group A children (124/190) than group B children (10/28, p=0.0027). In Group B, the mortality rate was very high (75%) (OR=16, 95% CI [5.79-45.90.], P<0.001) and concerned predominantly children under the age of 24 months (OR=0.08, 95% CI [0.01-0.47.], p=0.0017) and earlier (OR=0.21, 95% CI [0.03-1.25.], P=0.047).

**Conclusion:** Much remains to be done in countries with limited resources to improve pediatric HIV- treatment and survival, especially among the very young, which are weakened by childhood diseases. The implementation of WHO recommendations by the government must become a priority, this in order to improve the survival of affected children.

**Keywords:** HIV/AIDS; ARVs; Morbidity; Mortality; Child

## Introduction

According to the 2010 World UNAIDS report, expanding access to antiretroviral therapy has helped reducing the number of deaths among people living with HIV by 19% between 2004 and 2009 [1]. Definitely, major progress has been made concerning the HIV pandemic, as demonstrated by the >25% decline of the incidence of infection between 2001 and 2009 in 33 countries [1]. Still, HIV infection remains one of the leading causes of morbidity in childhood. It has increased infant mortality in the most affected countries and threatens to wipe out years of progress in the fight for child survival [2].

According to the AIDS Indicator survey of 2005 in Côte d'Ivoire, a country much affected by the HIV/AIDS pandemic in West Africa, HIV infection prevalence was estimated at 4.7% with 2.9% of men and 6.4% of women infected. This corresponds to 570,000 adults and children infected by the virus, including 350,000 females (61.4%) [3]. The number of children under 15 years old infected has increased from 50,000 in 2005 to 74,000 in 2013. Currently HIV prevalence in Côte d'Ivoire is estimated at 3.4% in children and adolescents <15 years. Only 15% of them are under ARV treatment [4].

Efforts to fight this pandemic were undertaken by the public pediatric healthcare services and included the provision of free antiretroviral treatment. In 2001, the first national evaluation of the situation of pediatric HIV took place. In 2005, decentralization of the health care activities allowed an increase from previously four to 175 pediatric HIV treatment sites in 2010 [5].

Wishing to provide care for HIV infected children, the Pediatrics Department of Cocody University Teaching Hospital (Centre Hospitalier Universitaire de Cocody, CHU-Cocody), one of the three teaching hospitals in the country's economic capital, Abidjan, and the

Elisabeth Glazer Pediatric AIDS Foundation (EFPAF) united forces to provide care. In this paper we shall give an overview of work conducted in this spirit and describe morbidity and mortality of the pediatric HIV-patients the department cared for.

## Resources and Methods

### Framework

The study has been conducted within the unit in charge of pediatric HIV in the CHU-Cocody in Abidjan. Since November 2005, a multi-disciplinary team involved in health care activities and in support of children living with HIV is in charge of the unit. The treatment of the pediatric HIV/AIDS is carried out according to national guidelines.

### Type and method of study

This retrospective study investigated care and outcomes of pediatric HIV-patients followed at the CHU-Cocody from November 28th 2005 to June 30th 2010 (5 years). HIV positive children- living or deceased with an exploitable patient file (file comprising the primary check-up and including all mentioned follow-up consultations) were included. Children lost to follow-up, thus who have not had contact with the center for at least 90 days and for which therefore outcomes cannot be defined, and those who have been transferred to other health care centers were excluded from analysis. The studied population was divided into two groups: Group A: all children under antiretroviral therapy and group B: all children without antiretroviral therapy, because they were still immune-competent, disqualified for the treatment for social reasons or had contraindications such as transaminases 10x higher than normal. According to the Ivorian national consensus in use from 2005 to 2010, the following children were eligible for ARV treatment:

- Children under 5 years old with a percentage of CD4<25% regardless of the WHO clinical state (CDC or WHO) or having a WHO clinical state 3-4 or CDC B-C and this regardless of the percentage of CD4.

- Children of 5 years and older who have a rate of CD4<15% or <200 cells/mm3 regardless of clinical state (CDC or WHO) or WHO clinical state 3-4, CDC B and C regardless of CD4.

The clinical monitoring was conducted quarterly. The initial assessment at admission and the semi-annual monitoring assessments covered full blood count, transaminases, creatin, glycemia and were carried out free of charge. Additionally, children were seen whenever they were sick.

### Data collection

Data were collected using a survey form including the following parameters: socio-demographic (sex, age, nationality, place of residence); clinical (reason for medical examination, medical history, physical examination at entry, nutritional status, CDC classification, diagnosis at admission), laboratory work-up information (Type of HIV, lymphocyte count, blood count), therapeutic (treatment regimens, Cotrimoxazole); and evolution and outcomes (Pathology during follow-up, severe morbidity which caused hospitalization or death).

### Data processing and analysis

Data entry was performed using MS Excel 2007. Data were analyzed with EPI Info 6.0. The population of children under ARV was compared to that of children without ARVs. Statistical tests used were the Chi 2, the Fisher exact test and Odds ratio. The significance level chosen was 5% and the confidence interval 95%.

## Results

Of the 336 children followed during the study period, 37 (11.0%) were transferred to another health care center, 81 (24.1%) children were lost to follow-up. 218 (64.9%) patient-files were selected meeting the inclusion criteria. Group A was made-up of 198 children and group B of 28 children.

### Characteristics of children at admission

The average age of children in group A was 66.11 months. These children were symptomatic in 84.74% of cases, presenting severe immunodeficiency in 54.74% and were under first line therapy combining 2IN (nucleotide inhibitors) + 1INN (non nucleotide inhibitors) in 86.31% of cases.

The children in the group B were younger with a mean age of 48.14 months, slightly symptomatic (60.7%) in the majority of cases and did not present with severe immunodeficiency.

The majority of children in both groups were infected with HIV-1. All children in group B (100%) and only 85.26% in group A received cotrimoxazole.

Patient history upon admission reviled different patterns in both groups. In Group A previous history of digestive problems (52.63%), dermatological concerns (46.84%) and tuberculosis (19.47%) were encountered, while previous pulmonary affections were more frequent in group B. The most frequent reasons for medical consultation at first presentation in group B were fever (57.86%) and coughing (55.26%). Physical examination mainly revealed pulmonary signs (54.21%) and alteration of general state (43.15%) in group A and oral candidiasis for children in group B. Bacterial pneumonia in addition to HIV was the most frequent medical diagnoses in both groups upon inclusion into the HIV-care-program. Table 1 and 2 show the main characteristics of children.

| Characteristics at the admission | Group A (n=190) | | Group B (n=28) | |
|---|---|---|---|---|
| | Amount | Percentage | Amount | Percentage |
| **Age (months)** | | | | |
| <24 | 66 | 34.73 | 8 | 28.57 |
| [24-60] | 32 | 16.84 | 5 | 17.86 |

| | | | | |
|---|---|---|---|---|
| >60 | 92 | 48.42 | 15 | 53.57 |
| **Sex** | | | | |
| Male | 93 | 48.94 | 15 | 53.57 |
| Female | 97 | 51.05 | 13 | 46.42 |
| **Type of HIV** | | | | |
| HIV1 | 184 | 96.94 | 28 | 100 |
| HIV2 | 4 | 2.10 | 0 | 0 |
| HIV1 + 2 | 2 | 1.05 | 0 | 0 |
| **Clinical stage (CDC)** | | | | |
| N | 10 | 5.26 | 8 | 28.57 |
| A | 19 | 10.00 | 9 | 32.15 |
| B | 60 | 31.59 | 7 | 25.00 |
| C | 101 | 53.15 | 4 | 14.28 |
| **Immunodeficiency** | | | | |
| Absent | 21 | 11.05 | 18 | 64.29 |
| Moderate | 65 | 34.21 | 10 | 35.71 |
| Severe | 104 | 54.74 | 0 | 0 |
| **ART** | | | | |
| First line | 164 | 86.31 | - | - |
| Second line | 28 | 13.69 | - | - |
| **Cotrimoxazole** | | | | |
| Yes | 162 | 85.26 | 28 | 100 |
| No | 28 | 14.73 | 0 | 0 |

Table 1: Characteristics of HIV-positive children at the admission.

| Clinical characteristics | Group A (n=190) | | Group B (n=28) | | OR | 95% [CI] | P |
|---|---|---|---|---|---|---|---|
| | Amount | Percentage | Amount | Percentage | | | |
| **Clinical History** | | | | | | | |
| Pulmonary | 37 | 19.47 | 13 | 46.42 | 0.07 | - | |
| Digestive | 100 | 52.63 | 8 | 28.57 | 2.78 | [1.09 to 7.26] | 0.001 |
| Dermatological | 89 | 46.84 | 2 | 7.14 | 11.46 | [0.02 to 0.28] | 0 |
| Tuberculosis | 37 | 19.47 | 0 | 0 | - | - | - |
| Neurological | 2 | 1.05 | 0 | 0 | - | - | - |
| Fever-going | 35 | 18.42 | 4 | 14.28 | 1.35 | | 0.78 |
| No medical history | 0 | 0 | 6 | 21.42 | - | - | - |
| **Reason for check-up** | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Hyperthermia | 110 | 57.86 | 6 | 21.42 | 5.04 | [1.83 to 14.61] | 0 |
| Coughing | 105 | 55.26 | 8 | 28.57 | 3.09 | [1.21 to 8.08] | 0 |
| Emaciation | 68 | 35.79 | 6 | 21.42 | 2.04 | [0.74 to 5.94] | 0.134 |
| Diarrhea | 49 | 25.79 | 3 | 10.71 | 2.90 | [0.78 to 12.62] | 0.131 |
| Paleness | 40 | 25.79 | 3 | 10.71 | | | |
| Rash | 39 | 20.52 | 5 | 17.85 | | | |
| **Clinical examination** | | | | | | | |
| Pulmonary signs | 103 | 54.21 | 8 | 28.6 | 2.96 | [1.16 to 7.74] | 0.011 |
| Trush | 85 | 44.73 | 20 | 71.4 | 0.32 | [0.12 to 0.82] | 0 |
| Poor general impression | 82 | 43.15 | 6 | 21.43 | 2.78 | [1.01 to 8.06] | 0.028 |
| Paleness | 60 | 31.54 | 4 | 14.28 | 2.77 | [0.86 to 9.88] | 0.09 |
| Polyadenopathy | 61 | 32.10 | 4 | 14.28 | 2.84 | [0.88 to 12.12] | 0.08 |
| Dermatosis | 36 | 18.94 | 6 | 21.43 | 0.86 | [0.30 to 2.56] | 0.755 |
| **Admission diagnosis** | | | | | | | |
| Bacterial pneumonia | 54 | 28.42 | 9 | 32.14 | 0.84 | [0.33 to 2.15] | 0.685 |
| Malaria | 29 | 15.26 | 6 | 21.43 | 0.66 | [0.23 to 2.00] | 0.279 |
| Severe acute malnutrition | 47 | 24.73 | 4 | 14.28 | 1.97 | [0.61 to 7.09] | 0.326 |
| Anemia | 31 | 16.32 | 3 | 10.71 | 1.69 | [0.45 to 7.50] | 0.304 |
| Tuberculosis | 3 | 1.58 | - | - | - | - | - |
| Shingles | 4 | 2.11 | - | - | - | - | - |
| *Deterioration of the General state; **Acute and severe malnutrition | | | | | | | |

**Table 2:** Clinical characteristics of children with HIV.

## Average period of monitoring

More than 2/3 (78.58%) of the children of group B were monitored for less than one year. The Average period of monitoring was 20.96 months for group A and 3.85 months for group B.

## Disease episodes during follow-up

In total, 764 disease episodes occurred during the follow-up; 633 in group A (mean 3.2 episodes/child) and 131 in group B (mean 4.7 episodes/child). Anemia (p=0.036) and pneumonia (other than tuberculosis) (P=0.011) were more frequent in group A. The main diseases encountered in both groups are listed in Table 3.

| Morbid events types | Group A (n=633) | | Group B (n=131) | | | | |
|---|---|---|---|---|---|---|---|
| | Amount | Percentage | Amount | Percentage | OR | 95% [CI] | P |
| Anemia | 166 | 26.22 | 23 | 17.55 | 1.67 | [1.07 to 2.79] | 0.036 |
| Oropharyngeal candidiasis | 50 | 7.89 | 10 | 7.63 | 1.02 | [0.49 to 2.25] | 0.918 |
| Bacterial pneumonia | 64 | 10.11 | 21 | 9.16 | 2.96 | [1.16 to 7.74] | 0.011 |
| Prurigo | 45 | 7.1 | 5 | 3.81 | 1.93 | [0.72 to 5.64] | 0.165 |
| Malnutrition | 36 | 5.68 | 3 | 2.29 | 2.57 | [0.75 to 10.64] | 0.164 |
| Malaria | 25 | 3.94 | 5 | 3.81 | 1.04 | [0.37 to 3.15] | 0.86 |
| Parotitis | 15 | 2.36 | 3 | 2.29 | 1.04 | [0.28 to 4.57] | 0.626 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Tuberculosis | 15 | 2.21 | 1 | 0.76 | 3.16 | [0.43 to 64.62] | 0.209 |
| Meningoencephalitis | 9 | 1.42 | - | - | - | - | - |

**Table 3:** Major morbid events listed during follow-up.

## Hospitalizations

Hospitalizations were more common in the children of group A (124/190) than the children in group B (10/28; p=0.0027). Severe acute malnutrition constituted the leading cause of hospitalization in both groups (29.03% vs 40%).

Table 4 shows all the inpatient diagnoses.

| Inpatient diagnoses | Group A | | Group B | |
|---|---|---|---|---|
| | Amount (n=124) | Percentage | Amount (n=10) | Percentage |
| Severe acute malnutrition | 36 | 29.03 | 04 | 40.00 |
| Pneumonia | 31 | 25 | - | - |
| Severe malaria | 21 | 16, 93 | 01 | 10.00 |
| Gastroenteritis | 26 | 20.96 | 01 | 10.00 |
| Severe anemia | 15 | 12.09 | 02 | 20.00 |
| Pneumocystis | 5 | 4.03 | 01 | 10.00 |
| Pulmonary tuberculosis | 2 | 1.61 | - | - |
| Bacterial meningitis | 2 | 1.61 | 01 | 10.00 |
| Cerebral toxoplasmosis | 2 | 1.48 | - | - |

**Table 4:** Selected inpatient diagnosis.

## Mortality

The mortality rate was higher in group B (75%) than in group A (15.79%) (OR=16, 95% CI [5.79-45.90], P=0). Fatal outcomes were more frequent in those under 24 months, especially in group B (43.33% of deaths in group A versus 90.47% in group B) (OR=0.08, 95% CI [0.01-0.47.], P=0.0017). Furthermore, in young children of group B, fatal events also occurred earlier with two thirds taking place less than six months from the date of registration (66.60% versus 90.50%) (OR=0, 21, 95% CI [0.03-1.25], P=0.047). The main causes of death in both groups were malnutrition (26.67% vs. 28.57%), followed by anemia (16.66% vs. 14.28%) and the diarrhea (13.33% vs. 19.05%) as displayed in Table 5.

The major causes of death are summarized in Table 5.

| Causes of death | Group A | | Group B | |
|---|---|---|---|---|
| | Amount (n=30) | Percentage | Amount (n=21) | Percentage |
| Malnutrition | 08 | 26.67 | 06 | 28.57 |
| Anemia | 05 | 16.66 | 03 | 14.28 |
| Diarrhea | 04 | 13.33 | 04 | 19.05 |
| Bacterial pneumonia | 01 | 3.33 | 03 | 14.28 |
| Pleural pneumopathy | 02 | 6.66 | 02 | 09.52 |
| Tuberculosis | 02 | 6.66 | 01 | 04.76 |
| Septicemia | 03 | 10.00 | 01 | 04.76 |
| Pneumothorax | 01 | 3.33 | - | - |
| Meningo – encephalitis | 01 | 3.33 | 01 | 04.76 |

| | | | | |
|---|---|---|---|---|
| Cerebral toxoplasmosis | 01 | 3.33 | - | - |
| Brain abscess | 01 | 3.33 | - | - |
| Acute renal failure | 01 | 3.33 | - | - |

**Table 5:** Causes of Death.

## Discussion

Despite the progress made in the fight against HIV/AIDS, diagnosis and HIV-infected children, treatment are still tardy in countries with limited resources. The average age of children in our study at admission was high; 5 years 7 months (66.11 months) in group A and 4 years 1 month (49 months) in group B. Kwara et al. [6] in Ghana and Ugochukwu [7] in Nigeria reported similar mean age (4.5 years and 4.78 years). The majority of children in group A (84.74%) and more than one third of children in group B (29.28%) were symptomatic.

The most frequent reasons for check-up in group A were fever and coughing. Clinical examination revealed primarily pulmonary symptoms, weakened general condition for group A, and oral candidiasis for Group B. Babatunde et al. [8] in Nigeria and Lodha et al. [9] in India had also described these signs in variable proportions. More than half of the children in group B had severe immunodeficiency (54.74%). Diack et al. in Senegal [10] and Kariyo et al. [11] in Burundi respectively reported in their series 57.14% and 84% of severe deficiency. Strategies such as AIDS Testing Advices Initiated by Health Care Service Providers must be implemented in all health facilities in the country. This will allow early and rapid mass HIV testing, and an instant treatment of HIV-infected children.

Results demonstrate that next to HIV, concerned children also need to fight other severe affections such as pneumonia, malnutrition, malaria, anemia and tuberculosis. Pulmonary manifestations are common in pediatric HIV infection. In fact, in group B, 46.42% of the children had a history of pulmonary disease and 54.21% of the children in group A, presented signs of pulmonary affections on physical examination at the time of admission. Bacterial pneumonia (non-tuberculosis) was a frequent diagnosis in both groups: 28.42% of children in group A and 32.14% in group B had pneumonia at first admission to the HIV-care-program and, 10.11% (group A) and, 9.16% (group B) during follow-up. Almost a quarter of the children in group B (24.19%) were hospitalized for a pulmonary affection. HIV infection is a major risk factor for invasive pneumonia [12]. The Identification of bacteria in pneumonia remains difficult. For Gray et al. [12] the relevant organisms are Pneumocystis jiroveci and gram-negative bacilli.

In our study, anemia was frequently observed during follow-up in group A (26.22%). Seventeen children were hospitalized for severe anemia (hemoglobin <5 g/dl). Anemia is commonly reported in HIV/AIDS-positive children [13-15]. Its origin is multifactorial: both, poor nutritional status of the HIV infected children and also the more or less combined in-take of ARVs (AZT) and cotrimoxazole may play a role [14].

Malnutrition in HIV-infected children is a public health priority and a challenge for African countries with limited resources. There is an undeniable link between HIV infection and malnutrition. Indeed, nutritional requirements increase during HIV infection and the presence of malnutrition promotes permanent morbid condition in infected children. Severe acute malnutrition was found in 24.73% of the children in group A and 14.28% of the children in group B on admission; it has persevered during follow-up, since 5.68% of children in group A and 2.29% in group B was still undernourished during follow-up visits. Severe Acute Malnutrition was the leading cause of hospitalization in both groups (29.03% and 40%). The work of Kimani Murage in South Africa [16] and Choudhary in India, on the nutritional assessment of a HIV-infected children population revealed prevalences of 18% of severe acute malnutrition, 12.9% among children under 5 years and 39.4% in those over 5 years [17]. The early HIV/AIDS testing and malnutrition treatment improves the quality of life of children living with HIV. Care activities and nutritional support are essential in the management of pediatric HIV infection. Sunguya et al. reported [18], the routine administration of Therapeutic Food Ready for Employment in children on ART significantly reduces the occurrence of malnutrition.

Co-infections of tuberculosis and HIV/AIDS are a reality in pediatric care. They represent a challenge due to their unusual clinical manifestations, difficult diagnosis and particularly high morbidity and mortality rates. In our study, 37 children (19.47%), all from group A, showed a history of tuberculosis and 19 children were treated for pulmonary and extra-pulmonary tuberculosis, either at admission (1.58%) or during follow-up. Immune Reconstitution Inflammatory Syndrome or IRIS was encountered in 16 children. Diack et al. [10] and Bugaje et al. [19] found themselves with higher rates of TB: with 16% and 45.7% of HIV-cases. It would be important to instaure a free and global treatment program of the co-infection TB/HIV in health facilities because even if there are free anti-TB and anti-retroviral drugs, clinical para-investigations are limited and still not available free of charge.

In Côte-d'Ivoire, malaria is highly endemic. While its severe form (P. falciparum) was responsible for 16.93% of hospitalization among children in group A versus 10% in group B, during follow-up, the incidence of malaria was similar in both groups (malaria responsible for 3.94% of morbid events in group A and 3.81% in group B). It is possible that the concomitant intake of the Cotrimoxazole is protective. That drug has been reported to have a beneficial role in preventing malaria in people living with HIV [20].

Severe acute malnutrition was the primary cause of death in both groups (26.67% and 28.57%). Adonis-Koffy et al. [23] found 36.70% deaths in their study whose causes were mainly due to the combination of the protein-energy malnutrition and of a secondary dehydration to a diarrhea in 27.40% of the cases.

Mortality over the five years of follow-up was less pronounced in group A (15.79%) than in group B (75%) (P<0.001). Although some of the children in group B were eligible for ARV treatment according to national guidelines (stage B (25%) and C (14.28%)), circumstances prevented their antiretroviral therapy implementation. This may have been due to the lack of active and conscientious parent involvement, the presence of a vital distress or of the transaminases increasing. This

explains the fact that some patients in group B at the WHO clinical state B did not receive ARV treatment despite their eligibility. Actually, a study by Camille et al. [21] in Togo showed a high and early mortality during the first 6 months of antiretroviral therapy.

The mortality rate was highest in the group of children aged less than 24 months (P=0.0017) in group B. Children under two years of age are indeed the population most at risk. Desmonde [22] reported that mortality rates were three times higher in children under 12 months than those older, before the introduction of ART.

Although instauring the prevention of mother to child transmission (PMTCT) of HIV seemed like a major hope in Côte d'Ivoire, its implementation still faces major difficulties. In 2011, according to the health statistics yearbook [5], only 404,443 mothers have been tested for HIV during their pregnancy with a positivity rate of 3.5% (14413 / 404443). The vast majority of children for a long time did not benefit from free PCR at 6 weeks of age, as this was only introduced in Côte d'Ivoire in 2011, thus after our study period. Their status therefore remained unknown.

Children under two years in particular, and all children under 5 years in general should benefit from early diagnosis and ARV treatment whatever the CD4 rate, according to the WHO 2013 recommendations.

The time to occurred death was shorter in group B (P<0.05). Only early antiretroviral therapy would inevitably reduce the mortality related to the HIV infection in children [24,25].

## Conclusion

The pathology associated with pediatric HIV infection is very rich, including pulmonary affections, malnutrition, malaria, anemia, and tuberculosis. Their importance depends on whether the child is on antiretroviral treatment or not. Lack of early ARV therapy is a major reason for the encountered high mortality in HIV-positive children under 24 months of age.

Much remains to be done in countries with limited resources to improve pediatric HIV treatments and care, especially among the very young that simultaneously have to fight many childhood diseases. The implementation of WHO recommendations by national governments must become a priority in order to improve the survival of children living with HIV.

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