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Original Research Article

Evaluation of the Survival of Children Infected with HIV Followed for 10 Years at the Pediatric Hospital of Kalembe-Lembe in Democratic Republic of Congo

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ABSTRACT

The causes of decreased survival of HIV children are dominated by immunosuppression in developing countries. But data on survival in sub-Saharan Africa are fragmentary. The overall goal was to assess the survival of HIV-infected children at Kalembe-Lembe Pediatric Hospital.
A prospective cohort study of HIV-infected children followed at the Kalembe-Lembe Pediatric Hospital between 2006 and 2015. Death was the criterion of judgment and children lost to follow-up were censored. The curves of Kaplan Méier made it possible to describe the survival of children at the threshold of $p < 0.05$.
Thirty-five children, including 20 girls (57.1%), median age 45.7 months, 22.9% at WHO stage 4 and 60% with psychomotor delay were included. 48.6% of the children had died. The probability of survival was 74.3% at 1 year, 68.6% at 2 years, 54.3% at 4 years, at 51.4% at 6 years and 45.7% at 10 years. The median survival time was 6 years (IEQ: 4.7-7.4). Stage 4 WHO, CD4 cell count <200 cells/µL, and psychomotor delay reduced the survival of HIV-infected children.
Decreased immunity in children and mental retardation are the poor prognostic factors for child survival in this cohort. Screening, early initiation of HART, and the fight against the retardation mental can increase the survival of children infected with HIV.

Keywords: Survival, Infected children, HIV, Psychomotor retardation, Kalembe-Lembe Pediatric Hospital

INTRODUCTION

Triple antiretroviral therapy (HART) has resulted in a significant decline in overall mortality in patients with human immunodeficiency virus (HIV) infection. [1-3] In the Democratic Republic of Congo (DRC), the HIV epidemic is of a generalized type with a prevalence in the general population estimated at 1.2%, [4] current estimates show that 381 187 people will live with HIV, of which 42,145 are children under 15 years of age. [5]

HART, available since the 2000s in our country, has enabled the care of children. However, despite adequate management with HART, adverse effects of the virus on the CNS are not completely reversible and neurodevelopmental and

cognitive disorders persist. [6-10] This persistence of neurodevelopmental and cognitive disorders is at the root of the high mortality observed in regional differences, with a decrease in survival in the world, especially in developing countries like the DRC. [11,12] The overall objective of this study is to evaluate the survival of HIV-infected children after 10 years of follow-up at Kalembe-Lembe Pediatric Hospital.

Patients and methods

This was a prospective cohort study from 2006 to December 2015. The children were recruited at the Kinshasa Reference General Provincial Hospital and followed in the cohort of the Kalembe-Lembe Pediatric Hospital for 10 years. The study population consisted of all HIV-infected children enrolled in the cohort and followed up at Kalembe-Lembe Pediatric Hospital until 2015. The primary outcome measure is death. Children lost to sight were censored.

Inclusion criteria: Any child aged 18 to 72 months, infected with HIV, naive or under treatment for less than one week. Children tested negative, those with HIV less than 18 months (non-availability of PCR in 2006) or beyond 72 months and those who were on treatment for more than one week were not included in the survey study.

The systematic examination of the children made it possible to obtain, from an ad hoc survey form, the essential information for this study.

Socio-demographic data:

Sociodemographic characteristics included age and sex at cohort recruitment. Clinical and biological data included weight, height, disease episodes, WHO stage, psychomotor development, children's CD4 count at enrollment, and vital outcome. Disease episodes included the number of times children could have fever, cough, and other symptoms requiring consultation. Opportunistic infections have also been part of these episodes. Nutritional status was assessed using the P /A index; T /A and P /T. Survival was defined as the period from the first day of recruitment of the child to the date of death for the deceased, the last assessment for the lost to follow-up, and at the end of the study (December 31 2015) for the survivors.

Statistical analyzes

The data has been entered and encoded using the Epi info 3.5 software. The data analyzes were performed using SPSS software version 21, the indices to assess the nutritional status were calculated using the ENA software. Descriptive statistics were presented as Median and EIQ, percentages and confidence intervals (95% CI) as appropriate. The Kaplan Meier method described survival between the date of recruitment of children and death (complete data) and the end of the study (censored data). Patients lost to follow-up at the end of the study (n = 2) were censored. The Log-rank test was used to compare the survival curves. A value of $p < 0.05$ was considered the statistical significance level.

Ethical considerations: The data was collected anonymously and confidentially. The privacy and the personality of the children have been safeguarded. The three fundamental principles of ethics were respected during the course of the study, namely: the principle of respect for the person, that of beneficence and that of justice.

RESULTS

General characteristics of children at enrollment

At enrollment, infected children had a median age of 45.7 months, severe acute malnutrition in 34.3% and chronic malnutrition in 54.3% of cases. It also shows that children were enrolled at an advanced stage of the disease in 54.3% in stage 3 and 22.9% in stage 4. Children had a retardation of severe psychomotor development in 60% of cases for development in 28% for motor development (Table 1).

Overall evolution of the subjects of the study

Vital issue during ARV follow-up Table 2 shows that 48.6% of children died during ART, and 5.7% were lost to follow-

up. Survivors accounted for 45.7% of cases (Table 2).

Evolution of annual disease episodes during ARV follow-up

Figure 1 shows that under ARV, the annual disease episodes have significantly decreased during the evolution under treatment (from 10 to 0 episodes per year).

Table 1. General characteristics of HIV + children at enrollment

Variable	n= 35
Age Me (Month)	45,7
Sex M n (%)	15(42,9)
P/A ≤ SD, n (%)	20(57,1)
T/A<- 2SD, n (%)	19(54,3)
P/T<-2 SD, n (%)	12(34,3)
CD4 Me(EIQ), /mm^3	767(559-994)
Stage OMS	
Stage 1	4(11,4)
Stage 2	4(11,4)
Stage 3	19(54,3)
Stage 4	8(22,9)
Mental development delay	
No	5(14,3)
Moderate	9(25,7)
Severe	21(60,0)
Motor development delay	
No	11(31,4)
Moderate	14(40,0)
Severe	10(28,6)

Table 2. Vital issue during follow-up

Vital issue	n	% (95%CI)
Survival	16	45,7(28,6-62,9)
Death	17	48,6(31,4-65,7)
Lost view	2	5,7(0,1-14,3)
Total	35	100,0

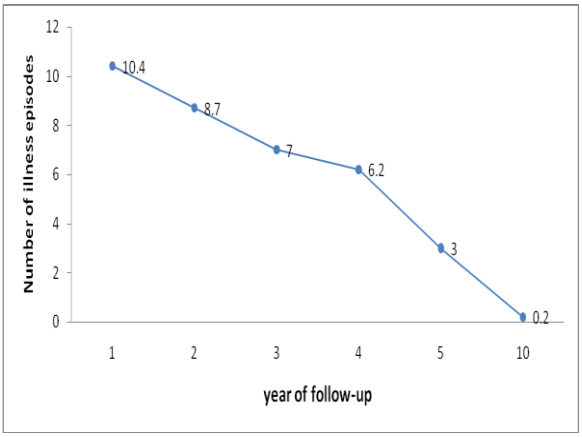

Figure 1.Evolution of disease episodes / year

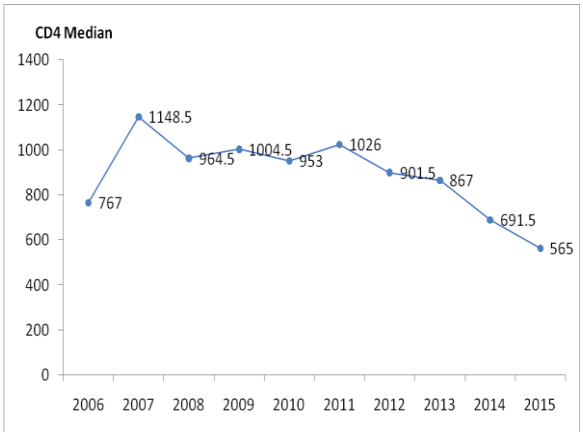

Figure 2. Evolution of CD4

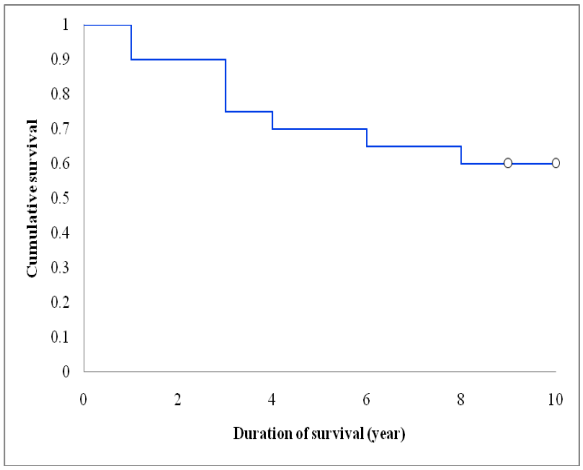

Figure 3. Probability of survival of children at 10 years of follow-up

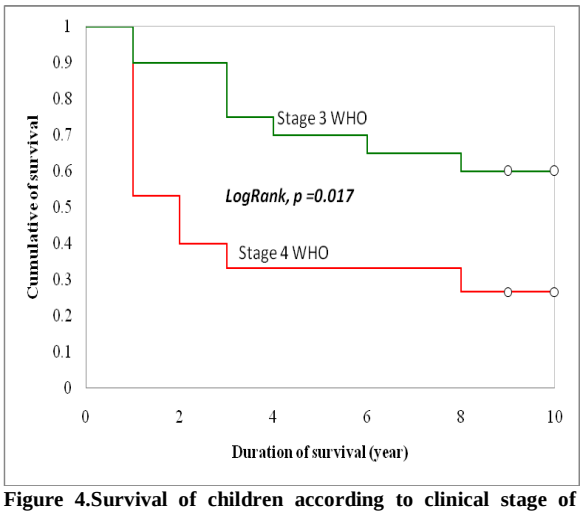

Figure 4.Survival of children according to clinical stage of WHO at enrollment

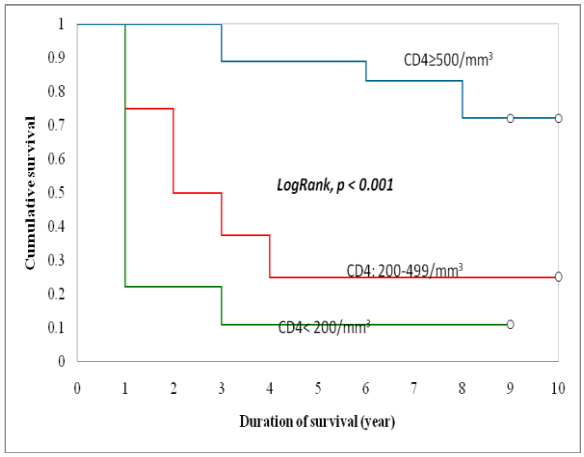

Figure 5.Survival of children by immunological status at enrollment

CD4 evolution of the subjects of the study

Figure 2 shows a stagnation of the absolute number of CD4 during evolution, there is a slight increase of CD4 in year 1 which will subsequently stagnate and regress without reaching the bar of 500 elements / mm3

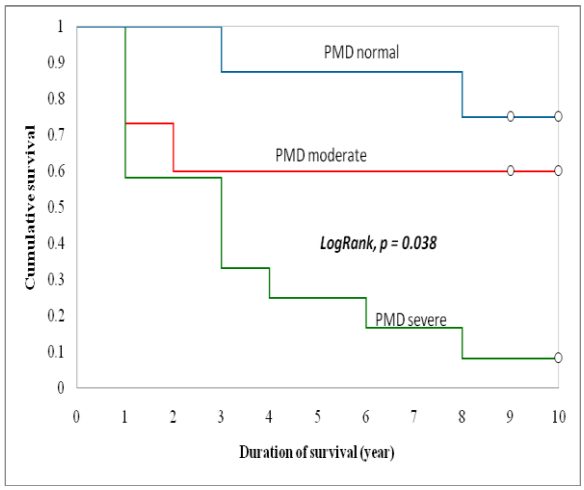

Figure 6.Survival of children by neurodevelopmental profile at enrollment

Overall survival of children

Probability of survival at 10 years of follow-up

The probability of survival was 74.3% at 1 year, 68.6% at 2 years, 54.3% at 4 years, at 51.4% at 6 years and 45.7% at 10 years. The median survival time was 6 years (IEQ: 4.7-7.4) (Figure 3).

Survival according to clinical stage of WHO at enrollment

The median survival at 10 years of follow-up is 4 years for children in WHO stage 4 and 7 years for stage 3 children with a statistically significant difference.

Survival of children by immunological status at admission

Survival is better in children with CD4 ≥ 500 / mm3 or a median follow-up of 8 years, compared with 4 and 2 years for those between 200 and 500 / mm3 respectively and those less than 200 / mm3 with a statistically significant difference (Figure 5).

Survival of children according to psychomotor development at admission

Survival is better in children with normal psychomotor development with a median follow-up duration of 6 years, compared with 4 years for those with moderate or severe delay, with a statistically significant difference (Figure 6).

DISCUSSION

The purpose of this study was to evaluate the survival of infected children who experienced psychomotor retardation early in their care.

In this series, children with HIV had a high incidence of severe psychomotor retardation, 60%. This finding was demonstrated in Annelies Van Rie et al. study in 2008 in a cohort in Kinshasa among children infected with HIV. [13] This high frequency of severe psychomotor retardation could be explained by the low rate of children on HART.

Our study shows that 48.6% of children died during the evolution under ARV, and 5.7% were lost of sight. Survivors accounted for 45.7% of cases. This same result also shows a stagnation of the absolute number of CD4 during the evolution with regression without reaching the bar of 500 elements / mm3. This situation could be at the root of a high frequency of HIV-related causes of death. The probability of survival was 74.3% at 1 year, 68.6% at 2 years, 54.3% at 4 years, 51.4% at 6 years and 45.7% at 10 years. The median survival time was 6 (IEQ: 4.7-7.4) years. During child follow-up, WHO clinical stage 4 reduced child survival by

73.3%. These results are consistent with several studies that have shown that the survival of HIV-infected children is related to the clinical stage of WHO characterized by a high frequency of opportunistic infections that may be at the basis of child deaths. [14-19]

In this study, CD4 count <200 cells / µL reduced child survival by 88.9%. In contrast, a better survival was found in children with CD4 ≥ 500 / mm3 or 8 years, against 4 and 2 years respectively for those between 200 and 500 / mm3 and those less than 200 / mm3.

This finding has been shown in several studies and found that CD4 ≤ 200 cells / µL during antiretroviral therapy was associated with high mortality, suggesting that critically immunocompromised patients still have an increased risk of death, even if they survive the first month of antiretroviral therapy. [20-22]

Survival is better in children with normal psychomotor development at 6 years, compared with 4 years for those with moderate or severe delay, with a statistically significant difference. In itself, neurodevelopmental delay is related to HIV progression and the clinical stage of children. According to UNICEF, [23] the correct and early care of HIV-infected children reduces the rate of psychomotor delay and subsequently increases survival.

Limitations of the studies.

This study has certain limitations. The study is primarily an observational cohort, so we cannot exclude the presence of unmeasured confusion. Then our study was conducted in a single center and the sample size is relatively small. As a result, our results may not be generalized across the country.

CONCLUSION

The results of our study showed that children who had a delay in one of their psychomotor development areas had lower survival than those who had normal development; this was also noted for those with severe immunosuppression.

Conflicts of interest

The authors declare no conflict of interest.

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Author Contributions

Conceptualization: MMA

Data curation: NNA

Formal analysis: NNA

Investigation: MMA

Methodology: MMA, PDC, NNA, NNC, AVR, TABP

Supervision: PDC, NNC, AVR, TABP

Validation: MMA, PDC, NNA, NNC, AVR, TABP

Visualization: MMA, PDC, NNA, NNC, AVR, TABP

Writing ± original draft: MMA, NNA, NNC

Writing ± review & editing: MMA, PDC, NNA, NNC, AVR, TABP

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