



ORIGINAL RESEARCH ARTICLE

Therapeutic and Evolutionary Aspects of Antiretroviral Treatment (ART) for Children in Libreville

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Abstract

Background: HIV remains a major public health problem worldwide. Without treatment, the disease progresses rapidly in children, half of whom die before the age of 2. The aim was to study the therapeutic and evolutionary aspects of HIV infection in children followed up in the various care centres.

Materials and methods: This was a retrospective study involving children followed up in paediatric CTAs in Libreville from January 2015 to December 2022. We included children aged 0-19 years with positive HIV serology or PCR. Statistical analysis was performed using SPSS version 25 software. The significance level was set at 5%.

Results: 288/345 cases were accepted, representing a participation rate of 83.5%. The mean age was 10.6 ± 5.1 years. The 10-14 age groups accounted for 32.3%. We had 84.6% of patients with moderate or severe immunity at entry. At ART initiation, 81.9% of our patients were on treatment and 19.1% were not. The 2INTI+INNTI (38.9%) and 2INTI + II (49%) combinations were the most commonly used. The drugs administered were Lamivudine (34%), Dolutegravir (23.6%), Tenofovir (26.4%) and Abacavir (17.7%). The course of treatment showed 92.4% follow-up, 2.8% deaths and 4.9% lost to follow-up.

Conclusion: HIV-AIDS in children remains a public health problem, given its socio-economic impact on the population. The high cost of follow-up tests and supply shortages are among the problems that slow down regular patient follow-up.

Keywords

HIV, Immunodeficiency, Antiretroviral, Child, Libreville

Introduction

Human immunodeficiency virus (HIV) infection is a chronic viral infection characterized by the progressive destruction of CD4 T lymphocytes. It is responsible for Acquired Immunodeficiency Syndrome (AIDS), which is the final stage in the development of HIV infection [1]. HIV infection remains one of the major causes of morbidity and mortality in children and adults worldwide. In 2022, UNAIDS estimated that 38.4 million people were living with HIV, 66% of them in sub-Saharan Africa [2]. The number of infected children and adolescents worldwide was estimated at 2.8 million, 88% of them in Africa [3]. Despite improvements in the coverage and effectiveness of Prevention of Mother-to-Child Transmission (PMTCT) interventions worldwide, the number of children under 15 living with HIV has risen from 1.5 million in 2001 to 3.5 million in 2010. The number of new infections among children and adolescents is estimated at 300,000 worldwide. Around 18% of HIV-related deaths occur in children [3]. Without treatment, the disease progresses rapidly in children, and half of them die before the age of 2 [3]. The main route of infection for children is vertical [4], with an additional risk from unprotected breast-feeding [5]. For more than 20 years, research has provided a better understanding of the mechanism of action of HIV and its persistence in the host organism. The advent of triple ARV therapy from 1996 onwards has reduced

mortality among patients living with HIV and the rate of mother-to-child transmission (MTCT) [6]. In 2021, more than 28.7 million PLHIV were on antiretroviral therapy (ART) worldwide. PLHIV on ART accounted for 36% of the 32.6 million PLHIV in these countries. Since 2010, new HIV infections among children have fallen by 52%. There are still problems with screening, diagnosis and access to treatment for infected infants. According to the WHO, many cases go undiagnosed. Only 43% of infants exposed to HIV have been screened and have access to ART. In Gabon, the HIV prevalence rate is estimated at 3.6% of the general population. Nearly 2,500 children are affected according to the latest epidemiological surveillance bulletin from UNAIDS Gabon, and only 587 children are currently known and receiving care [7]. By 2025, 95% of all people living with HIV (PLHIV) should have been diagnosed, 95% should be on life-saving antiretroviral treatment (ART) and 95% of PLHIV on treatment should have their viral load suppressed, both to improve their health and to reduce future HIV transmission. Given the paucity of studies on this condition in children in Gabon, and in order to help improve paediatric care, we proposed to carry out this study, the main objective of which is to evaluate the therapeutic and evolutionary modalities of HIV infection in children followed up in all the major paediatric care centres in Libreville.

Materials and Methods

This was a retrospective, descriptive and analytical study from January 2015 to December. It took place in Libreville. This is Gabon's most populous city. The study was conducted in 4 facilities in the capital: the Centre de Traitement Ambulatoire (CTA) pédiatrique de Libreville, CHU Mère Enfant Fondation Jeanne Ebori (CHUMEFJE), the CTA de Nkembo, and the Hôpital d'Instructions des Armées Omar Bongo Ondimba (HIAOBO). The study population consisted of HIV-positive children aged between 2 months and 19 years who were being followed up at these facilities. The sample was non-probabilistic and exhaustive. Inclusion criteria were: positive HIV serology or positive HIV PCR according to age of diagnosis, aged 0-19 years, and complete medical records. Data were collected from patient follow-up records using a pre-established standardised form. The variables studied were sociodemographic data (age, sex, parents' social status, personal and family history), clinical data (nutritional status, opportunistic infections, and clinical status), biological data (viral load, CD4 count, and pre-treatment work-up), treatment (date treatment started, drugs used, and changes in treatment) and outcome (duration of follow-up, regularity of follow-up, death). Data entry and statistical analysis were performed using Excel 2013 and SPSS version 25. Qualitative variables were expressed as headcount and frequency, and quantitative variables as mean and standard deviation (or median). Comparisons

between categorical variables were made using the Chi² test (or Fisher for small numbers) and comparisons of means by the Student test. The significance level was set at 5%. All administrative authorizations within the aforementioned structures were obtained.

Results

During the study period, 345 patients were recruited and 288 met the inclusion criteria, giving a participation rate of 83.5%. The sex ratio was 1.13, with males predominating (53.1%; $n = 153$). The mean age was 10.6 ± 5.1 years, with extremes of 2 months and 19 years. The 10-14 age groups accounted for 32.3%. The Libreville CTA accounted for 55.6% of patients recruited and the CHUMEFJE for 21.2%. 65.3% ($n = 188$) of the children attended school and 47.6% were behind in their schooling. They were orphans (46.9%; $n = 135$), 105 of whom were maternal orphans (36.5%) (Table 1). The head of the family was unemployed in 39.6% of cases. Parents with an average income numbered 151 (52.4%), while those with low and high incomes numbered 106 (36.8%) and 31 (10.8%) respectively. PMTCT had not been carried out in 97.2% of cases ($n = 280$). Patients were referred in 53.5% of cases for a positive VRS, 7% of cases for an opportunistic infection and 39.6% of cases for mothers suspected of being HIV-positive. The circumstances of discovery were dominated by long-term fever (40.6%), tuberculosis of any location (13.2%), with pulmonary involvement in (11.2%). Patients at clinical stage 3 accounted for 27.8% and at stage 4 for 5.2% (Table 2). At the last consultation, these figures fell to 5.9% for both groups combined. After initiation of ART, 186 patients (64.6%) had an undetectable viral load (ULV) and 49 of these had a detectable ULV (17%), with extremes ranging from 1,040 to 7,310,000 copies/ml. Fifty-three patients (18.4%) had no CV. The mean CD4 count rose from $554/\text{mm}^3$ to $674/\text{mm}^3$, with maximums ranging from 3039 to 2159. We had 214 patients (84.6%) with a CD4 count of less than $1000/\text{mm}^3$, corresponding to moderate or severe immunosuppression at the initial consultation. This rate rose to 79.5% after initiation of treatment. Also, 15.4% of patients had a CD4 count $> 1000/\text{mm}^3$ compared with 20% after treatment. In addition, 35 patients (12.1%) had not had their CD4 count checked at the initial consultation, and this figure rose to 35.7% of patients after the start of treatment. The pre-treatment work-up was without abnormality in 54.9% of cases. 40.6% had an abnormal work-up and 2.8% had no work-up. In 69.8% of cases, patients received their treatment immediately (< 10 days). The prescription was delayed in 10.1% of patients. The main reason for the delay in administering treatment was waiting for the pre-treatment assessment. In 58.9% of cases, this wait was between 10 and 30 days, and more than 30 days in 20.5% of cases. The triple therapy most commonly used when initiating ART was the 2INTI + INNTI combination in 38.9% of cases. The 2INTI + II

combination represented 49% of triple therapy at the last consultation. We had 19.1% of patients without treatment (Table 3). At ART initiation, the drugs used were Lamivudine (34%), Dolutegravir (23.6%), Tenofovir (26.4%) and Abacavir (17.7%) (Figure 1). No change of molecule was made in 62.68% (n = 146). And in 29.2% (n = 68), the reason for the change was the unavailability of the drug in the country (Table 3). Treatment follow-up was regular for 78.9% of patients. 20.1% had discontinued treatment and 1% had irregular follow-up. Opportunistic infections were absent in 87.8% of cases in the 1st trimester of ART and in 72.2% after one year. Patients were rarely hospitalised while on ART. Two hundred and fifty-six cases (88.9%) were not hospitalised, 23 (8%) only once and 9 (3.1%) more than twice. After initiation of ART, we recorded 8 deaths

(2.8%), 14 patients lost to follow-up (4.9%) and 266 patients (92.4%) in follow-up. There was an association between the number of opportunistic infections and the duration of ART (p < 0.001). Orphan children were significantly more likely to discontinue treatment than non-orphans (p = 0.044).

Discussion

HIV infection in children is a public health problem in sub-Saharan Africa. We conducted this study to update our data and improve care for HIV-positive children in Gabon. However, we were confronted with several difficulties, in particular the unexploitation of certain medical records, the retrospective nature of the study, and the failure to interpret CD4 counts according to their percentage as required by international standards.

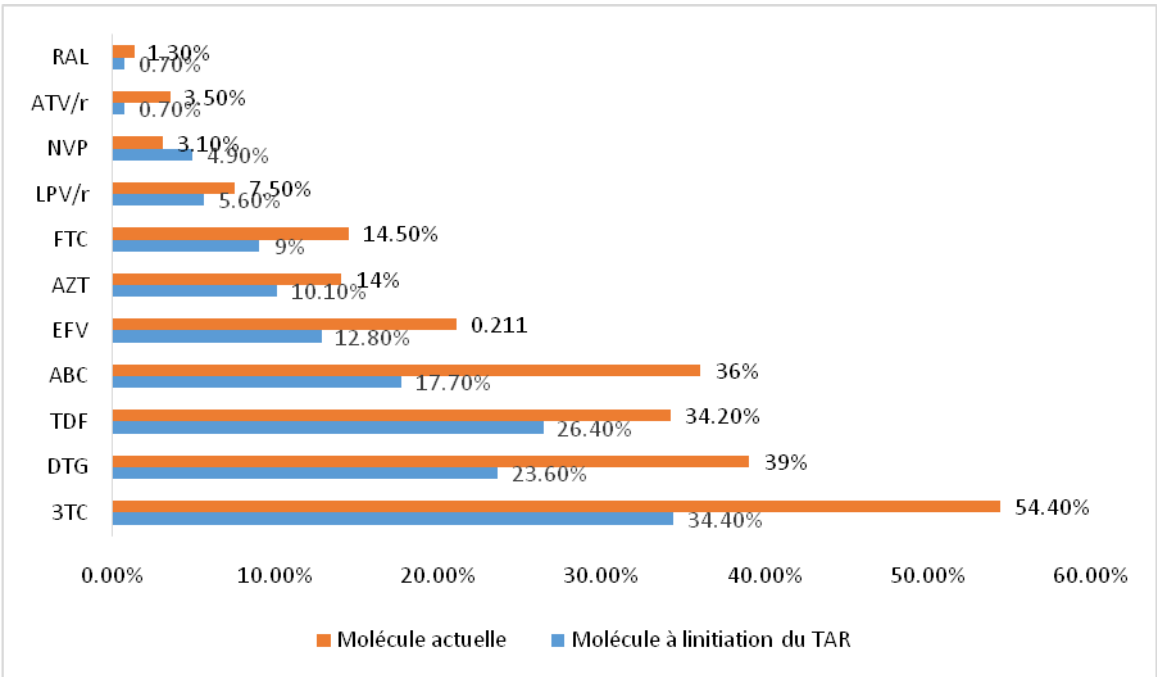


Figure 1: Breakdown of the population by drug used.

Table 1: General characteristics of the study population.

Parameters	Workforce (n)	Percentage (%)
Age (year)		
0-4	44	15.3
5-9	76	26.4
10-14	93	32.3
15-19	75	26.0
Grade level		
Academic delay	137	47.6
Not in school	56	19.4
Normal schooling	50	17.4
In advance	44	15.3
Not specified	01	00.3
Orphan status		
No	153	53.1
Yes	135	46.9
- Mother's	105	36.5
- From father	09	3.1
- The 2 parents	21	7.3

Table 2: Clinical data.

Parameters		Workforce (n)	Percentage (%)
Circumstance of discovery	Fever	117	40.6
	Chronic cough	54	18.8
	Under nutrition	20	6.9
	Diarrhea	17	5.9
	Chronic anemia	9	3.1
	Maternal serology	69	24.0
Co-infection	Pulmonary tuberculosis	25	8.7
	Lymphnode tuberculosis	06	2.1
	Multifocal tuberculosis	03	1.0
	Digestive involvement	11	3.8
	Dermatological involvement	09	3.1
	Neurological involvement	03	1.0
	ENT involvement	07	2.4
	Malaria	04	1.4
	None	220	76.4
WHO Stadium	1^{ère} consultation		
	1	145	50.3
	2	48	16.7
	3	80	27.8
	4	15	5.2
	Last consultation		
	1	240	83.3
	2	31	10.8
	3	14	4.9
	4	3	1.0

Table 3: Therapeutic data.

Parameters	Workforce (n)	Percentage (%)
Trither		
2INTI + INI	109	37.8
2INTI + INNNTI	112	38.9
2INTI + IP	66	22.9
INTI + IP + INI	1	0.3
Current tripple therapy		
2INTI + INI	141	49.0
2INTI + INNNTI	42	14.5
2INTI + IP	46	15.9
INTI + IP + INI	2	0.7
No TAR	57	19.7
Reason for change		
No change	146	62.6
National unavailability	68	29.2
New recommendations	12	5.2
Therapeutic failure	2	0.8
Intolerance	3	1.3
Adaptation to weight and age	2	0.9
Reasons for delayed treatment		
Pre-therapeutic assessment pending	58	79.4
Out of sight	3	4.1
Out of stock	2	2.8
Anti-TB treatment	9	12.3
Anti TB treatment + Out of sight	1	1.4

The mean age of the children were 10.6 ± 5.1 years, with extremes ranging from 2 months to 19 years. The 10-14 age groups represented 32.3% of the study group. Kobangue [6] in the Central African Republic found a lower mean age of 6.5 years, with extremes ranging from 4 months to 15 years. Cissé [8] in Senegal had lower results than us, with a mean age of 8 years and extremes ranging from 6 months to 19 years. Tshikwey Ngwey [9] in the Democratic Republic of Congo found an average age of 9 years, with extremes ranging from 3 to 15 years. This study shows a clear pattern of late diagnosis, with an average age of 10 years, and at the same time early detection and management of patients. The youngest patient on ART was 2 months old. This early diagnosis is due to the introduction of early screening in all delivery and newborn care centres.

We noted a male predominance (53.1%) with a sex ratio of 1.13. This male predominance was found in Morocco [10], Botswana [11] and Zimbabwe [12] at 53.1%, 52.4% and 50.5% respectively. Traore in Mali [1] and Luque [13] in Latin America found a female predominance of 76.3% and 53% respectively. These studies show that HIV AIDS affects patients of both sexes in almost similar proportions.

In 53.5% of cases, patients were referred with a positive VRS, and in 39.6% of cases, this was due to family screening. Other authors such as Thiam [14], Ismail [15] and Rizkou [10] also found family screening in 24%, 28.5% and 40% respectively. These results can be explained by the fact that there are not many paediatric referral centres for HIV. Paediatric clinics are the main referral centres for this disease. The paediatric CTA only opened its doors in 2015. Children in Greater Libreville were mainly referred to the general hospital (CHUL). The pre-treatment work-up was without anomaly in 158 patients (54.9%). Anaemia was found in 29.2% of cases. The study by Kobangue [6] found anaemia in similar proportions (33.9%). For Thiam [14], Diancoumba [16] and Prakash Poudel [17] these figures were higher at 65%, 64.86% and 74.4% respectively. This significant difference could be explained by the size of the different studies. With the exception of Kobangue's study and our own, the other three had fewer than 100 patients. There is therefore a greater probability of having a concentration of anaemic patients. However, we can also see that anaemia plays an important role in the manifestations of HIV/AIDS in children, intertwined with the nutritional deficiencies they suffer. This once again underlines the qualitative importance of nutritional intake in this care. We had 214 patients (84.6%) with moderate to severe immunodeficiency and a CD4 count of less than $1000/\text{mm}^3$ at the initial consultation. After initiation of treatment, 79.5% of patients had a moderate to severe immune deficiency, showing a decrease in this rate. Similarly, the CD4 count increased,

with the proportion of patients with a CD4 count $> 1000/\text{mm}^3$ rising from 15.4% to 20% after initiation of ART. At the time of the first consultation, 35 patients (12.1%) had not had their CD4 count checked. This figure tripled after the start of ART to 35.7% ($n = 103$), showing that these patients had difficulty carrying out follow-up tests, which are sometimes costly. Takassi [18] and Diancoumba [16] found respectively 84.6% and 77% of moderate or severe immunodepression, figures similar to ours. TshikweyNgwey [9] and Kalla [19] had higher figures with a moderate or severe immunosuppression rate of 95.2% and 91.6% respectively. The absence of immunosuppression was found respectively in TshikweyNgwey [9] and Diancoumba [16] in 11.3% and 24.4%. Our study found similar results at 15.4%. Immunodeficiency once again reflects the age and rapidity of HIV infection in children. All studies agree on this point. ART improves this deficit by restoring the CD4 count to normal. This is the main objective of ART, which is to reduce or even eliminate the number of opportunistic events, thereby improving survival and quality of life in children. After initiation of ART, 64.7% of patients ($n = 186$) had an undetectable viral load. This is corroborated by Barry in Guinea Conakry [20] who found 89.8% undetectable viral load. However, Barro Makoura [21] and Thiam [14] found respectively 45.3% and 77.8% of detectable CV in their studies. Controlling viral load is an integral part of assessing good adherence to treatment. Regularly taking ART leads to an increase in CD4 count, a fall in viral load and, consequently, clinical improvement. The results of these studies carried out in West Africa show that patients have easier access to these follow-up check-ups, which is the result of a free-of-charge policy implemented in these countries.

In our study, 62.6% of patients received their treatment immediately. In fact, ART followed correctly and for a long time is the source of an improvement in the CD4 count, which will slow down or prevent the onset of opportunistic infections, thereby improving the patient's clinical condition and prolonging his or her life.

Patients were rarely hospitalised while on ART. Two hundred and fifty-six cases (88.9%) were not hospitalised and 32 (11.1%) were hospitalised at least once. Traoré in Mali [22] found a hospitalisation rate of 33%, three times higher than in our study. This difference may be explained by a study population in which there was a higher rate of opportunistic infections. In the case of HIV-positive patients, the number of hospitalisations is linked to the number of opportunistic infections. This population is more susceptible to opportunistic infections (OIs) and therefore to frequent hospitalisations. The aim of ART is to reduce the number of OIs and hence hospital admissions. Our study shows that well-monitored ART reduces the number of hospitalisations. After initiation of ART, we recorded 8 deaths (2.8%), 14 patients lost

to follow-up (4.9%) and 266 patients (92.4%) in follow-up. Diancoumba [16] and Takassi [18] respectively had a survival rate of 62.2% and 93.81% compared with 5.4% and 5.29% of deaths. Diouf [23] found 83% survivors compared with 15.7% deaths. The case-fatality ratio in these studies was higher than in our own, which may be explained by better follow-up, although lost to follow-up could increase these figures.

Conclusion

HIV/AIDS remains a major public health and socio-economic development problem throughout the world and in sub-Saharan Africa in particular. Interesting progress has been made at national level in the care of HIV-infected children, in particular the setting up of CTAs in general and paediatric CTAs in particular, although there are still not enough of them. The 10-14 age group has been the most affected. There have been delays in initiating ART due to waiting for the results of the pre-treatment assessment. 2INTI+INNTI and 2INTI+II were the main protocols. In 29.2% of cases, the lack of ARV stocks was the reason for a change of protocol. Mortality was 2.8% with a survival rate of 92.4%.

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Conflicts of Interest

All authors declare that they have no conflicts of interest in this publication.

Authors' Contribution

All authors participated in carrying out the study.

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