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Original Research Article

Factors associated with viral suppression and rebound in children and adolescents living with HIV on antiretroviral treatment at the Bangui pediatric complex, Central African Republic

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ABSTRACT

Background: Suppression of viral load and its maintenance is the necessary condition for reducing mortality linked to HIV infection in children. This study aimed to investigate the factors associated with viral load rebound in children receiving antiretroviral treatment.
Methods: This was a cross-sectional study with analytical purposes, running from August 1 to 31, 2023. Were inclusive, all children living with HIV under 15 years of age, with at least two viral load results and whose parents have agreed to participate in the study.
Results: A total of 286 children were included in the study. The mean age was 11.5 years (±2.8). More than half (55.2%) of the children were not informed of their HIV status and for the majority (50.3%). Among the 198 children with a suppressed viral load at the first test, 46 (23.2%) experienced a rebound in viral load at the last test. The factors significantly associated with rebound were the low level of education of the parents (p=0.012), the administration of medicines to the children by the parents (p=0.000), the long duration of taking the medicines (p=0.021) and poor compliance with treatment (0.000).
Conclusions: The rebound in viral load after suppression is a disastrous reality for children. Efforts must be made to strengthen early therapeutic education for children, training of health workers on the process of announcing results and ongoing dialogue with children and adolescents on compliance are ways to improve the maintenance of viral suppression.

Keywords: Bangui, Child, Rebound viral load

INTRODUCTION

According to UNAIDS data, 39 million people are living with HIV infection worldwide.[1] Thanks to antiretroviral therapy (ART) there is a reduction in morbidity and mortality linked to HIV infection. With a view to eliminating HIV infection by 2030, UNAIDS has set global targets "95-95-95" in 2021. The third "95" placed emphasis on eliminating HIV infection. Viral load, a necessary condition for reducing morbidity and mortality linked to HIV infection.

In the Central African Republic (CAR), there are an estimated 124,732 (95,100; 184,874) the number of people living with HIV in 2022 including 11,512 (8371; 16263) children aged 0 to 14. The number of child deaths is estimated at 1276 in 2022.[2] According to the "95-95-95" cascade, 36.5% of children living with HIV know their status, 36.5% of children knowing their status are on antiretroviral treatment and 22.4% of children on treatment have a suppressed viral load.[2] Since 2021, the national AIDS control program has adopted a new first-line therapeutic regimen based on the combination of dolutegravir for children and adolescents and raltegravir for newborns.

To improve the quality of life of children living with HIV, viral load suppression must be maintained for as long as possible. This requires good compliance with treatment and support for children on antiretroviral treatment. In children, long-term treatment success is complicated by compliance issues, limited pediatric drug formulations, changes in body mass requiring modifications in drug doses, and sharing of HIV status results with the child.[3]

The WHO has developed tools to facilitate treatment compliance in children and new pediatric formulations of antiretrovirals have been developed. Despite the reduction in morbidity and mortality, a considerable proportion of patients fail to achieve a durable virological response to treatment.[4] In CAR, no study has been carried out on a durable virological response in children.

It is in this context that our study aimed to study the factors associated with the rebound of the viral load in children receiving antiretroviral treatment and to identify the associated factors.

METHODS

Setting and type of study

The study was carried out at the outpatient treatment center (CTA) of the Bangui pediatric complex, which is the reference structure for the care of children in CAR. This was a cross-sectional study with analytical purposes, running from August 1 to 31, 2023.

Study population

The study population constituted children living with HIV followed at the CTA of the pediatric complex.

Inclusion and exclusion criteria

Any child living with HIV aged 6 weeks to 15 years, with at least two viral load results, whose parents have agreed to participate in the study was included. Children whose parents have not agreed to participate in the study were excluded.

Study population and sampling

We opted for an exhaustive recruitment. Any child meeting the inclusion criteria and seen in consultation during the study period was included.

Variables

The main variables studied were:

Dependent variable including viral load. The viral load is suppressed when it is less than 1000 copies/ml, it is not suppressed when it is greater than 1000 copies/ml according to WHO recommendations.[5]

Explanatory variables were age, gender, parental education level, orphan status, duration of treatment, clinical stage at initiation, date and results of viral load, level of compliance, treatment regimens at initiation, change of treatment, disclosure of HIV status, method of drug administration.

Collection of data

Participants were recruited during children's treatment renewal visits after their informed consent. The data were collected using an individual questionnaire designed and previously tested for clarity and length; and also through patient records.

Data analysis

The data has been entered and analyzed using Epi info version 7 software. The chi-square test was used to compare proportions. A p value <0.05 was considered statistically significant. Measures of association were estimated by the odds ratio (OR) and their 95% confidence interval (CI). The variables which have a significant link with the variable to be explained were introduced into a logistic regression model.

Ethical consideration

The study was carried out in strict compliance with the Declaration of Helsinki, which states that no intervention that could alter the dignity, integrity and right to privacy of the participants was carried out. Verbal consent was obtained from each participant prior to the interview and completion of the questionnaire. Each participant was assured that his or her refusal would not affect his or her treatment. The data were treated with strict confidentiality.

RESULTS

A total of 286 children were included in the study. One hundred and ninety-eight had a suppressed viral load at first test and 88 had an unsuppressed viral load. The figure below shows the distribution of children at the first and second viral load tests.

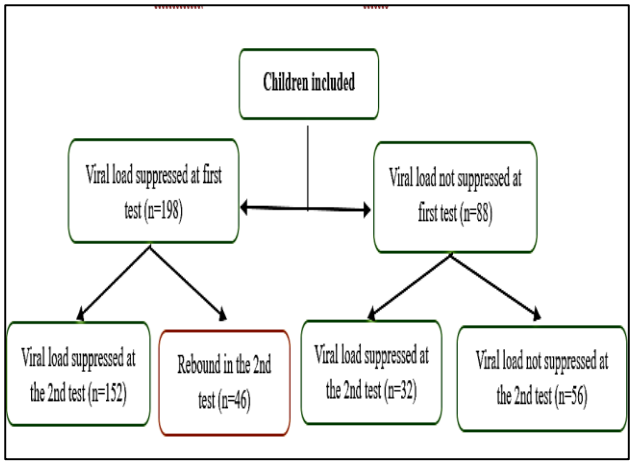

Figure 1: Distribution of children at the first and second viral load test.

Socio-demographic characteristics

Of the 286 registered, boys were the majority (55.2%). The mean age was 11.5 years (±2.8), the youngest at 3 years and the oldest at 14 years. Most of the children were at primary school level (69.9%). Approximately, 41.3% of children have both living biological parents and 24.5% were orphans of both father and mother. Finally, most of the people caring for children are at secondary level (67.1%). Details of sociodemographic characteristics are in Table 1.

Table 1: Distribution of participants according to their sociodemographic characteristics.

Item	Numbers (n=286)	%
Age in year		
<10	68	23.8
≥10	218	76.2
Sex		
Boy	158	55.2
Girl	128	44.8
Educational level of children		
Secondary	78	27.3
Primary	200	69.9
Maternal	4	1.4
Unschooled	4	1.4
Existence of biological parents		
Both parents are alive	118	41.3
Both parents are deceased	70	24.5
Only the father is alive	50	17.5
Only the mother is alive	48	16.7
Educational level of caregivers		
Superior	40	14.0
Secondary	192	67.1
Primary	50	17.5
Unschooled	4	1.4

Clinical and therapeutic characteristics

Of the 286 children included, more than half (55.2%) were not informed of their HIV status. At the initiation of treatment, most children were at WHO clinical stage 1 (34.3%) or 2 (28.7%). The main treatment regimens at initiation were combinations based on nevirapine (46.2%) and lopinavir/ritonavir (34.3%). During the investigation, all patients were placed back on a combination based on dolutegravir. For most of the children (50.3%), it was their parents who administered the treatment. Finally, 66.4% of these children were declared observant (Table 2).

Table 2: Distribution of participants according to their clinical and therapeutic characteristics.

Item	Numbers (n=286)	%
Announcement of HIV seropositivity		
Yes	128	44.8
No	158	55.2
WHO clinical stage at treatment initiation		
Stage 1	98	34.3
Stage 2	82	28.7
Stage 3	62	21.7
Stage 4	44	15.4
Therapeutic regimens at initiation		
Nevirapine-based combination	132	46.2
Efavirenz-based combination	52	18.2
Combination based on lopinavir/ritonavir	98	34.3
Combination based on dolutegravir	4	1.4
Administration of treatment		
By parents	144	50.3
By the child himself	142	49.7
Duration of treatment in years		
2-6	64	22.4
6-10	132	46.1
10-14	90	31.5
Compliance with treatment		
Yes	190	66.4
No	96	33.6

Factors associated with viral load rebound

Among the 198 children with a suppressed viral load at the first test, 46 (23.2%) experienced a rebound in viral load at the last test. The factors significantly associated with rebound were the low level of education of the parents (p=0.012), the administration of medicines to the children by the parents (p=0.000), the long duration of taking the medicines (p=0.021) and poor compliance with treatment (0.000). Details can be found in Table 3.

Table 3: factors associated with viral load rebound (n=198).

Determinants	Bounce (n=46)	No rebound (n=152)	Gold (95% CI)	P value	ORa (95% CI)	P value
Age in year						
<10	32	114	1		-	-
≥10	14	38	0.76 (0.37-1.58)	0.463		
Sex						
Male	28	86	1	0.606	-	-
Female	18	66	1.19 (0.61-2.34)			
Parental education level						
Never and primary	14	24	1	0.027	1	0.012
Secondary and higher	32	128	2.33 (1.09-5.01)		2.71 (3.69-5.47)	
Existence of biological parents						
Both parents are alive	20	70	1	-	-	-
One of the parents is alive	18	52	0.83 (0.39-1.71)	0.607		
Both parents are deceased	8	30	1.07 (0.43-2.70)	0.884		
Announcing HIV test results						
Yes	16	62	1		-	-
No	30	90	0.77 (0.39-1.54)	0.465		
Medication administration						
By parents	34	64	1	0.000	1	0.000
By the child	12	88	3.89 (1.87-8.11)		3.01 (2.34-6.87)	
Duration of treatment in years						
2-6	10	46	1	-	1	-
6-10	5	70	3.04 (0.98-9.48)	0.047	2.17 (0.69-5.64)	0.258
10-14	21	36	0.37 (0.15-0.89)	0.024	0.41 (0.22-0.71)	0.021
Compliance with treatment						
Yes	10	98	1	0.000	1	0.000
No	36	54	0.15 (0.07-0.33)		0.29 (0.12-0.69)	

DISCUSSION

The present study was carried out to determine the proportion of children living with HIV who experienced a rebound in viral load after suppression and the factors associated with this rebound. In this study, the proportion of children with virological failure at the first test was 30.8%. Among those who had suppressed viral load at the first test, 23.2% experienced a rebound. Pediatric virological failure is a recurring problem in resource-limited settings.[6-8] If children fail to maintain optimal viral suppression and experience a rebound, this could compromise the quality of their lives with an increased risk of mortality.

In this study, gender and age were not significantly associated with viral load rebound. Some studies have found links between viral load dynamics and these two variables[9,10] others have found the opposite.[9-12]

Level of education is a parameter that influences health decisions. The low level of education of parents was identified by our study as a determinant of viral load rebound. It is certain that if parents do not fully understand how to take medications, this could be the cause of poor compliance, which is the main cause of non-suppression or rebound of the viral load. Orphan status can be the cause of mental and psychological instability in children infected with HIV which instability can lead to poor compliance.[13] This study did not highlight a link between orphan status and the rebound in viral load. This could be explained by the fact that the majority of children have at least one living parent. For the few who are double orphans, they are usually cared for by a family member.

According to the Morlat report, it is advisable to begin the process of informing the child about their HIV status from school age, favoring gradual information, adapted to the child's maturity and questions.[14] This could make it easier for the child to adhere to treatment as soon as he or she reaches adolescence. In our study, 55.2% of children were not informed of their HIV status. This could be explained by parents' feelings of guilt and the lack of competent personnel in the field of child psychology. Toolkits have been designed to facilitate the disclosure of HIV status to children.[15]

In this study, for the majority of children (50.3%), it is the parents who are responsible for managing medications and the administration of medications to children by parents

was identified by the study as a determinant of the rebound of viral load. Therapeutic education sessions must be set up for children from preschool age (3 to 6 years old) with the use of adapted tools in order to help them learn to recognize their medications. From school age, they will be able to manage their medications.[16] The business of parents and also that of school-aged children could lead to forgetting to take medication. A study conducted in South Africa showed that many caregivers of HIV-infected children used coercion and threats of serious consequences for non-compliance as a communication strategy to enforce compliance.[17] This is all the more important when children are not informed of their HIV status.

Compliance with treatment is a crucial element for the success of treatment. Our work found a significant link between non-compliance with treatment and the rebound in viral load. Which corroborates the results of several authors.[18-21] The duration of treatment is a determinant of viral load rebound in our study. Children often struggle to maintain sustained adherence over time, hence the need to support patients and their caregivers in developing strategies for long-term adherence to antiretroviral therapy.[22]

Our study has some limitations. We did not take into account factors such as the level of initial viral suppression or the level of immunosuppression which are also factors that could be at the origin of the rebound. However, these results will be useful for clinicians and those responsible for the AIDS control program to improve the maintenance of compliance, a necessary condition for the persistance of viral suppression.

CONCLUSION

The rebound in viral load after suppression is a disastrous reality for children. The low level of education of parents, the duration of treatment, the administration of medications by parents and poor compliance are all factors that determine this phenomenon. Efforts must be made by the national AIDS control program to strengthen early therapeutic education for children, training of health workers on the process of announcing results and ongoing dialogue with children and adolescents. On compliance are ways to improve the maintenance of viral suppression.

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