

Audits of Death in HIV-Infected Children and Adolescents Followed up in the Pediatric Department of the Regional Teaching Hospital of Borgou/Alibori from 2005 to 2020

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Abstract

Introduction: Human immunodeficiency virus (HIV) is a major public health problem with high morbidity and mortality among children. The objective of this work was to audit the deaths of children and adolescents with HIV infection followed up in the pediatric department of the Regional Teaching Hospital of Borgou/Alibori (CHUDB/A) the from 2005 to 2020. **Patients and Method:** This was a retrospective and descriptive study conducted in the pediatric department of CHUD/B-A in Parakou. All children with HIV infection who died from January 1, 2005 to August 31, 2020 were included. Data collection was carried out in three stages: a phase of medical records processing, a phase of community survey and a phase of death audits. The variables studied were sociodemographic, clinical, biological, therapeutic and evolutionary. **Results:** Over the study period, the data of 464 infected children were recorded, including 92 deaths, representing a case fatality rate of 19.83%. Severe acute malnutrition (69.23%), gastro-intestinal tract infections (43.58%) and serious opportunistic pulmonary infections (24.36% pulmonary tuberculosis and 19.23% pneumocystis) were the main causes of death. The main dysfunctions found were: the delayed diagnosis of HIV infection (79.35%), the absence or delay in consultation when the child's clinical condition deteriorates (32.61% and 47.83%), delayed initiation of antiretroviral treatment (42.39%) and non-adherence to treatment (38.04%). Non-adherence to treatment was predominant in adolescents (90.49%). **Conclusion:** Specific interventions for early detection, adequate nutritional care, psychosocial support for adolescents and mothers of children are necessary to reduce mortality due to HIV among

children and adolescents.

Keywords

HIV, Death, Children, Adolescents, Dysfunctions, Benin

1. Introduction

Human immunodeficiency virus (HIV) represents one of the major public health problems in sub-Saharan Africa. In 2019, 38 million people were living with HIV worldwide, including 4.9 million in West and Central Africa [1]. Over the years of response to this condition, a delay has been observed in meeting the needs of children and adolescents living with HIV [2]. However, they are the invisible part of the iceberg and are heavily impacted by this pandemic. In 2016, there were an estimated 2.1 million children and adolescents living with HIV worldwide, including 820,000 in West and Central Africa with 51,000 deaths in this region [2]. This trend is constantly increasing with an annual increase of 15% in the number of AIDS-related deaths among adolescents [2] [3].

Although Benin is classified as a country with a generalized epidemic of low prevalence in Africa, 2010 children under 14 years of age were on antiretroviral (ARV) treatment in 2017 with 258 deaths in this population [4]. Adedemy *et al.* in a study at the regional teaching hospital of Borgou/Alibori (CHUD-B/A) observed a mortality rate of 25.8% among HIV-infected children and adolescents in 2018 [5]. Improving access to antiretrovirals does not seem to control the mortality of children and adolescents living with HIV [2] [3] [6]. In this context, it is important to better understand the determinants of mortality in HIV-infected children and adolescents. The objective of this study was to audit the deaths of children and adolescents infected with HIV and followed up at the CHUD-B/A from 2005 to 2020 in order to improve their management.

2. Patients and Methods

This was a retrospective and descriptive study conducted in the pediatric department of the Regional Teaching Hospital (CHUD-B/A) of Parakou in Benin. It focused on children (0 - 9 years) and adolescents (10 to 21 years) with HIV infection, followed up in the department and who died during the period from January 1, 2005 to August 31, 2020.

Children under the age of twenty-one, confirmed positive for HIV infection on the basis of a positive PCR and/or HIV serology, having received antiretroviral treatment or not, followed up and then died in the department during the study period were included. Children suspected of HIV infection for whom biological evidence had not been made before death were excluded. Patient recruitment was exhaustive.

Data collection was carried out in three phases: a first phase of identification

of patients meeting our inclusion criteria, based on the examination of registers, the active search for those lost to follow-up and the collection of sociodemographic, clinical, paraclinical and evolutionary data. The sociodemographic data were: the age, gender and social status. Patients aged 0 to 9 years were considered children and adolescents were those between 10 and 21 years old. WHO considers children of 10 - 19 years to be adolescents, but in the cohort, some were between 19 and 21 years old. For an overall analysis of the cohort, the latter were included in the adolescent group. The clinical data were: clinical stage at the time of inclusion, initial nutritional status and during follow-up, opportunistic diseases, disclosure of the status to the child. The paraclinical data were: the type of HIV, HIV status of their parents, CD4 lymphocyte count and the viral load. Evolutionary data were the regularity and duration of follow-up, adherence, therapeutic failure and vital status during the study.

The second phase consisted of a verbal autopsy in the community with consenting parents or people responsible for the follow-up of the children. This phase allowed the collection of testimonies and additional information on the clinical status of children or adolescents, psychosocial experiences, and individual factors related to the deterioration of their clinical status.

The third phase was the audit of each death, based on all the data collected. This was a systematic qualitative analysis of cases based on predefined criteria, using a grid developed for this purpose. This analysis was carried out by a group of practitioners (pediatricians, nurses, social workers), specialists in HIV management. The data collected at this phase made it possible to identify the determinants of death, that is to say the attributability to HIV, the contributing factors of diagnostic and therapeutic nature linked to the socio-family, economic or psychological environment.

Death was considered attributable to HIV when the direct cause of death was an opportunistic disease or a direct consequence of HIV. The contributing factors selected were all events or disease that directly or indirectly and negatively affected the management process: screening, initiation of antiretroviral treatment, follow-up of patients until death.

All variable information was collected using a survey form. The data were entered into the EPIDATA software version 3.1 and analyzed using STATA 14 software. Central tendency parameters of qualitative variables were expressed as percentages and the quantitative ones as mean with standard deviation when the distribution was normal and by the median or its interquartile range (IQR) otherwise. The study was carried out after obtaining the favorable opinion of the ethics committee of the University of Parakou under the reference 0332/CLERB-UP/P/SP/R/SA.

3. Results

3.1. Death Rate

Over the period study, 464 children and adolescents with HIV infection were

followed up in the department. Among them, 183 (39.43%) were still in our active records, 140 (30.17%) were lost to follow-up, 49 transferred (10.56%) and 92 died, representing 19.83%.

3.2. Sociodemographic Characteristics

The average age of children at the time of discovery of HIV infection was 42.96 ± 6.15 months with the extremes of 1 and 176 months. The sex ratio was 0.8. Children whose HIV positive status was discovered between 12 and 60 months were the most represented (41.30%). The average age of children at the time of death was 73.04 ± 8.67 months with the extremes of 4 months and 254 months (21 years). Children aged between 12 and 60 months at death were the most represented (40.21%). Adolescents represented 21.34% of cases. **Table 1** shows the distribution of HIV-infected children according socio-demographic characteristics.

3.3. Clinical and Paraclinical Characteristics

Mother-to-child transmission was the main route of transmission found in 76 children and adolescents, or 82.61% of cases. Sexual route of transmission was noted in only one child and the transmission through blood in two children. For the rest of the cases the route of transmission was indeterminate. The majority of

Table 1. Distribution of HIV infected children according to socio-demographic characteristics.

	Size (N = 92)	%
Age (months)		
<12	18	19.57
[12 - 60]	37	40.20
60 - 120	16	17.39
>120	21	22.83
Sex		
Male	41	44.57
Female	51	55.43
Origin		
Parakou	71	77.17
Out of Parakou	21	22.83
Education Level		
None	57	61.96
Primary	15	16.30
Secondary	14	15.22
Superior	1	1.09
Out of school	5	5.43
Total	92	100.00

children were in advanced clinical stages when included in the follow-up cohort with 26 (28.26%) in WHO stage 3 and 52 (56.52%) in WHO stage 4. The immunological status was poor in the majority of patients at the start of their follow-up with 45.65% of children having a severe immunodeficiency.

3.4. Treatment-Related Characteristics

Among the children, 65 (70.65%) had received anti-retroviral therapy (ART) and 29.35% of them had not received it. In the group of children put on treatment, 36 had regular follow-up (55.38%) and 29 had not (44.62%). In terms of adherence to ART, 38.46% were compliant and 61, 46% were not. The average duration between the start of ART and non-adherence was 20.10 ± 04.88 months with the extremes of 1 to 99 months.

3.5. Knowledge of HIV Status by Children and Its Sharing with a Third Party

In this study, the HIV status was known to 17 children and adolescents (18.47%). Among them, 8 were under 15 years old when their status was announced (47.06%). The average age at full disclosure of HIV status was 14.64 ± 1.41 years with the extremes of 12 and 18 years. The HIV status was shared with other people apart from the person responsible for monitoring the child in 13 cases (14.13%).

3.6. Characteristics Related to Death

Deaths occurred at home in 53.26% of cases. The average time between discovery of HIV and death was 136.02 ± 14.43 weeks (02.62 ± 0.28 years) with the extremes of 0 and 811 weeks (0 and 15.60 years).

3.7. Direct Causes of Death

The cause of death was unknown in 14 children (15.22%) and severe acute malnutrition was found in 69.23% of the known causes, followed by gastrointestinal infections (43.5%) and pulmonary infections, including tuberculosis (24.36%) and pneumocystis (19.23%). **Table 2** shows the distribution of children included in the study according to direct causes of death.

3.8. Analysis of Dysfunctions

The main dysfunctions were as follows:

The absence or delay in consultation during the deterioration of the child's clinical condition was identified as the main dysfunction in 80.34% of all cases studied, followed by the delayed diagnosis of children. HIV infection, accounts for 79.35%. Delayed initiation of ART and poor adherence then occurred in 42.39% and 38.04% of cases, respectively (**Table 3**). Among adolescents, poor adherence (90.48%), and the absence or delay in consultation during the deterioration of the clinical status (90.48%) was the main dysfunctions at the origin of deaths.

Table 2. Direct causes of death in HIV-infected children and adolescents.

	Size (N = 78)	%
Causes of death* (N = 78)		
Severe Acute Malnutrition (SAM)	54	69.23
Gastro-intestinal tract infection	34	43.58
Tuberculosis (TB)	19	24.36
Pneumocystis	15	19.23
Lymphoid interstitial pneumonia	9	11.54
Dehydration	5	6.41
Sepsis	5	6.41
Severe pneumonia caused by common organisms	5	6.41
Severe malaria	3	3.85
Severe anemia	3	3.85
Neuromeningeal cryptococcosis	2	2.56
Mediastinal lymphoma	2	2.56
Cerebral toxoplasmosis	1	1.28
Immune reconstitution inflammatory syndrome	1	1.28

*Several causes can be associated in the same patient.

Table 3. Main dysfunctions leading to death for all cases.

	Size (N = 92)	%
Dysfunctions*		
Delayed diagnosis of HIV infection	73	79.35
Delayed initiation of ART	39	42.39
Poor adherence to ART	35	38.04
Irregular clinical follow-up	28	30.43
No confirmation of complication	19	20.65
Absence/delay in consultation when the complication occurs	74	80.43

*Several dysfunctions can be found in the same case.

3.9. Causes of Dysfunction

The causes of delayed diagnosis of HIV infection were the delayed consultation (91.78%) and screening in the face of suspicious manifestations in peripheral care structures (71.23%). As for poor adherence, it was mainly due to low commitment from the person responsible for the monitoring (71.43%). In the particular case of adolescents, tiredness of being under ARVs (63.16%) was associated with some other causes.

The delayed consultation when the clinical condition deteriorates, was mainly linked to weariness of parents or guardians in the face of multiple hospitalizations and a lack of financial means (90.54%) (**Table 4**).

Table 4. Causes of the main dysfunctions leading to death for all cases.

	Size	%
Late diagnosis of HIV infection (N = 73)		
Absence/Irregularity of PMTCT follow-up	17	23.29
Delayed consultation of symptomatic child	67	91.78
Delayed screening in the face of suspicious manifestations	52	71.23
Delay in initiation of treatment (N = 39)		
Loss to follow-up after diagnosis	16	41.03
non-availability of pre-therapeutic or eligibility assessment	25	64.10
Poor adherence (N = 35)		
Occupation of the responsible parent	17	48.57
Useless because of satisfactory status of health	3	8.57
Child tired of taking daily medication	13	37.14
Fear of being seen using ARVs	6	17.14
Lack of food	6	17.14
Lack of social support/Death of a parent	5	14.29
Depression	8	22.86
Poor commitment from the responsible person	25	71.43
Poor commitment from patients	14	40.00
Non-sharing of HIV status	8	22.86
Ignorance of the benefits of taking ARVs	8	22.8
Irregular clinical follow-up (N = 28)		
Problem of financing the trip	6	21.43
Opposition from spouse or other family member	3	10.71
Occupation of the responsible person	10	35.71
Poor commitment from the parent responsible for monitoring	22	78.57
Absence/delay at consultation when the complication occurs (N = 74)		
Weariness in the face of multiple episodes of hospitalization	67	90.54
Lack of financial means	31	45.74

4. Discussion

This was a retrospective and descriptive cross-sectional study which focused on all HIV-infected children followed up in the pediatric department of CHUD/B/A and who died in the period from January 1, 2005 to August 31, 2020. The exhaustive census of children made it possible to reduce possible biases related to the selection of medical records. In addition, the active search for patients lost to follow-up carried out during the present work made it possible to have a better estimate of the mortality rate. The retrospective nature of the study did not make it possible to collect all the information relating to the children, particularly

those relating to the circumstances of death in children who died in the community. But thanks to surveys carried out in the community and interviews with health workers, some data were able to be completed. In addition, the audit sessions allowed a review of each case with all the health staff, which made it possible to eliminate possible errors in transcription or interpretation of the data collected in the medical records.

The death rate of 19.83% in this study although high is certainly underestimated given the large number of patients lost to follow-up and not found despite the active research. High mortality rates are also reported by other authors in sub-Saharan Africa, notably 24.2% in Cameroon [7], 15.17% in Ivory Coast [8] and 18% at Cotonou in Benin [9] with significant number of patients lost to follow-up. This contrasts with mortality of less than 1% in developed countries [10] [11]. This observation demonstrates that the management of HIV infection in the population of children and adolescents remains a problem in our context. Early detection is a fundamental condition for increasing the chances of survival in this population [12]. In our study, the average age at the time of screening was 42.96 months. This age is late, since vertical transmission was the main route of transmission in children (82.6%). This delay in screening is that perceptible because most children and adolescents had a degraded clinical condition when the infection was discovered, with 28.26% classified in WHO stage 3 and 56.52% in WHO stage 4. This demonstrates the collapsed immunological status with almost half of patients experiencing severe immunodeficiency at the time of diagnosis. The late discovery of the infection associated with an advanced clinical stage have been reported by many authors in sub-Saharan Africa [7] [13] [14] [15], contrary to what is observed in developed countries where Frange *et al.* reported an average age of 22.8 months at the time of discovery [16].

In the present study, 29.35% of children had not received any antiretroviral treatment. Several studies, including in sub-Saharan region, report rates of ARV initiation varying from 90% to 100% [8] [12]. This difference is explained by the fact that we took into account all children, including those in the cohort before the 2010s in whom ART had not started on time. And it was after these years that thanks to the START study, the systematic treatment of HIV infection was generalized [17]. Other authors who took patients into account over the same period reported similar results [9] [15] [18].

The causes of death were divided into 3 groups: acute malnutrition (69.23%), gastro-intestinal tract infections (43.58%) and pulmonary infections (24.36% for pulmonary tuberculosis and 19.23% for pneumocystis). Nguefack *et al.* also reported malnutrition as the leading cause of death in HIV-infected children [19]. This is explained by the fact that HIV infection maintains a vicious circle, favoring the onset of acute malnutrition in affected patients, which malnutrition aggravates the immunodeficiency and promotes the occurrence of infections, particularly digestive and pulmonary infections [20]. This data is important to take into account in our disadvantaged context because it shows the importance of interventions in the sense of systematic screening and management of malnutri-

tion in children and adolescents living with HIV.

At the end of the analysis of the deaths, a continuum of dysfunctions that can be intertwined in the same child or adolescent emerges. Children infected with HIV in our context are subject to late diagnosis and treatment, irregular follow-up most of the time and non-adherence to treatment related to problems in their psychosocial environment.

Indeed, the dysfunctions begin from a delayed screening which is favored by three main events: the delayed consultation, absence of screening of symptomatic children in healthcare structures and finally the irregular monitoring of prevention of mother-to-child transmission (PMTCT). In the Beninese context and more broadly in sub-Saharan Africa, the classic therapeutic route is first self-medication then recourse to traditional healers [21], thus delaying the time of admission to the health center. Moreover, there is an absence of systematic screening found in 71.23% of cases. According to Oga *et al.*, the lack of HIV testing in pediatric departments would be due to the low acceptability of this test by mothers of children for fear of stigmatization of their spouses if the result was confirmed positive [22]. We could also mention the low specificity of symptoms, particularly in the early stages, leading some caregivers not to request serology [23]. All of these events represent missed opportunities for an early detection in order to improve the chances of survival of these children. The delayed initiation of treatment is now less alarming thanks to the new guidelines of HIV management which now require the initiation of ART as early as possible, whatever the clinical stage with available and free drugs in Benin [24].

The third type of dysfunction was related to the irregularity of clinical follow-up and especially to non-adherence to treatment. In our study 58.46% of patients were non-compliant. The impact of this poor adherence is that noticeable because the average of patients died within a sufficient time to reverse the deterioration of their immunological status (2.62 years between diagnosis and death). In sub-Saharan Africa, studies on adherence to ART in pediatric cohorts report non-adherence rates varying from 10% to 25% [25] [26]. The gap with our study could be explained by the fact that our population consisted only of deceased patients.

In the present work, the reasons for the non-adherence were multiple and revolved around the socio-cultural and psychological consequences of HIV-related stigma. Good adherence depends largely on the responsible adult. This commitment is lacking in our context where 71.48% of non-adherence is observed. Cissouma *et al.* made the same observation in Mali with proportions of non-adherence varying between 46% and 100% [26]. The verbal autopsies allowed us to link this situation to the refusal of the adults responsible for monitoring, mainly the mothers of children to share the serological status of their children with other people in their entourage. This is for fear of arousing suspicion about their own status. This leads them to give the medicines in secret to the patients, thus increasing the number of omissions and sometimes treatment discontinuation.

In the particular case of adolescents, the causes of non-adherence were: a poor commitment of adolescents to take the treatment (47.37%), ignorance of the benefits of taking ARVs (36.84%), depression (42.11%), fear of being seen regularly consuming ARVs (26.32%) and lack of social support (26.32%). All these reasons have their roots in the late disclosure or absence of disclosure of the diagnosis, associated with the climate of secrecy and fear of stigma related to the infection which prevents the adolescent from finding the necessary support from his or her family and his peers in his usual circle of life. All the parents of deceased adolescents who were interviewed during verbal autopsies reported a certain social isolation of the adolescent. This situation was also reported by Trocmé *et al.* in non-adherent adolescents forced to keep the secret of their infection in order to have an apparently normal life [27].

Finally, the last dysfunction, which was the delayed consultation when the child's clinical condition deteriorates and leads to death, was linked to weariness of parents in the face of repeated hospitalizations and lack of financial means. Multiple HIV complications and their management are financially and emotionally taxing for parents. In our country where there is no universal health insurance coverage and where psychological support is in its infancy, it is difficult for parents of infected children and adolescents to cope with all these constraints. Sometimes, they give up in the face of repetitive complications that can be fatal for the child.

5. Conclusion

This study allowed us to establish the continuum of dysfunctions to which HIV-infected children and adolescents are subject. It will serve as a basis for improving policies and services offered to this vulnerable population in order to reduce the deaths of HIV-infected children in our context.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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