

Pediatric HIV Infection in Togo: Situation of Child Care in the Central Region from 2008 to 2015

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Abstract

This piece of work covers thirteen (13) AIDS assistance programs sites over the period 1st January 2008 to 31st December 2015. The study is retrospective, descriptive, and cross-sectional based on 292 clinical cases of HIV infected children aged between 0 and 14 years old. A regional committee was charged to validate antiretroviral treatment (ART) prescriptions on a weekly basis. We have also used data from the regional committee register. HIV infected children represent 5.1% of casework on ART. The average starting age for ART was 4.5 years (1 - 180 months) with a sex ratio (Male/Female) of 0.9. The clinical classifications according to WHO guidelines were: Stage III (52.3%) and Stage IV (20.3%). The most frequent opportunistic infections were: wasting (40.12%), digestive candida infection (29.0%), acute respiratory infections (22.8%) and skin diseases (17.9%). The HIV type 1 was detected on all of the children (100%). The average rate of CD4 at the beginning of the ART was 552.98 cells/mm³, leading to a severe immuno-suppression in many cases (44.8%). The initial ART was essentially NEVIRAPINE + LAMIVUDINE + STAVUDINE. HIV infections diagnosis are usually late in the Central Region of Togo and will therefore be improved by the UNAIDS 90-90-90 strategic plan by 2020, through various initiatives. These are: the Prevention of Mother to Child HIV Transmission (PMTCT), the Early Infection Diagnosis (EID) based on Polymerase Chain Reaction (PCR) and the Provider Initiated Testing and Counseling (PITC).

Keywords

HIV, AIDS, ART, Children, Togo

1. Background

In 2014, 36.9 million people were living with Human Immunodeficiency virus (HIV) worldwide [1]. At the end of 2013, only 23% of needing children (<15 years) against 37% of adults were taking ART (Antiretroviral therapy) in the developing world. About 90% of these children come from Sub-Saharan African countries [2]. However, new pediatric infections decreased to 58% from 2000 to 2014 worldwide [1]. Also UNAIDS elaborated a strategy to decrease those prevalence rates further by 2020 with 3 targets: 90% of HIV infected children will be tested and their serological status be known by their parents; 90% of infected children will take ART over their lifetime; and 90% of those who are taking treatment should attain an undetectable viral charge [1].

In Togo, the HIV prevalence among the general population is 2.5% [3]. The children on ART (7% of casework on national records) were 3058 in 2015 [4]. Despite the rapid expansion of the Prevention of Mother To Child Transmission of HIV (PMTCT) services and the improvement of ART coverage on children population, the pediatric HIV infection care is insufficient in Togo. During the last fifteen years, PMTCT helped to prevent nearly 1,400,000 children from developing AIDS [2]. But stock-out of Polymerase Chain Reaction (PCR) tests, high rate of pregnant seropositive women lost of view in PMTCT program, lack of pediatricians, insufficiency of child care programs integration and the low task shifting limit the pediatric ART coverage improvement [4]. Several studies on the infected children have been performed in Togo [5] [6], but none of them focus on the Central Region. Therefore, the purpose of this investigation is to describe epidemiological, clinical, biological and therapeutic characteristics of HIV infected children in the Central Region of Togo from 2008 to 2015.

2. Methodology

Togo is a western African country, situated in Gulf of Guinea. Its population is about 6,191,155 habitants, with 51.4% of Women in 2010 [7]. The country is divided into five (5) administrative and six (6) health regions. The following work relates to the Central Region. Its population was about 696,020 habitants in 2015 for a geographical area of 13,307 km² [8]. The city of Sokodé, the administrative headquarter of that region is located 340 kilometers to the North of Lomé, the capital city of Togo. All the AIDS assistance programs sites (n = 13), looking after HIV infected patients in the Central Region, were included in the study. This work is a retrospective and cross-sectional study conducted from 1st January 2008 to 31st December 2015. We accessed 292 children clinical files from both the 13 facilities and the register of ART regional committee. This elected com-

mittee has the responsibility to scrutinise every patient medical reports and validate the prescriptions given by physicians, before the patient starts the ART. The committee meets on a weekly basis. The diagnosis of HIV infection follows definitions from WHO guidelines and other national policies [9] [10]: HIV exposed infant with PCR positive or presumptive clinical signs under 18 months, or a serological test negative after 18 months (Table 1). Patients aged more than 15 years, HIV exposed children with a PCR negative or a negative serologic test, and infected children without ART indication were not selected. A number of data items were collected: e.g. socio-demographic (age, sex, year of enrolment), clinical (WHO classification, type of opportunistic disease), biological (Type of HIV, CD4 rate, hemoglobin rate, creatinine, alanine aminotransferase) and therapeutic (ART regimes). The morbidity analysis was performed using the statistical software SPSS. A comparative statistical analysis was made according to the age. Tests of significance Chi-2 of Pearson or exact test of Fisher for qualitative data ($p < 0.05$) and Mann Whitney/Wilcoxon test for quantitative data were used. A multivariate regression analysis was performed in order to evaluate the role of the confounding factors on ART initiation. In this retrospective study using clinical files and registers, the patient's identity was not collected on the survey file as to guarantee ethical clearance.

3. Results

- **Epidemiologic estimates**

Table 1. National ART guidelines in Togo, 2010-2014 (National AIDS control program/Togo).

NATIONAL GUIDELINES	2010	2014
Pre-ART test	HIV Presumptive clinical signs Positive serological test after 18 months or positive PCR under 18 months	HIV Presumptive clinical signs Positive serological test after 18 months or positive PCR,
	CD4 rate, hemogram, transaminases (ALAT)	CD4 rate, hemogram, transaminases (ALAT)
ART eligibility criteria	WHO stage III or IV OMS CD4 rate < 20%	<u>Under 5 years</u> Treat all <u>after 5 years</u> WHO Stage III or IV Or CD4 rate < 350 cell/mm ³
	<u>Mother receiving NVP in PMTCT</u> d4T/3TC/NVP AZT/3TC + EFV Puis en 2011 AZT/3TC/NVP	<u>Under 3 years</u> ABC/3TC + LOP/r si âge 3 ans <u>From 3 to 10 years</u> ABC/3TC + EFV si 3 - 9 ans
First-line regimens	<u>Mother receiving not NVP in PMTCT</u> ABC/3TC + Lop/r	<u>Up to 10 years</u> TDF/3TC/EFV si plus de 10 ans
Second-line regimens	AZT/3TC + NFV ABC/3TC + LOP/r	ABC/3TC + LOP/r

From January 2008 to December 2015, the ART committee of the Central Region has received 292 clinical files of HIV infected children. The proportion of children initiating ART was 5.1% (292 out of 5,725).

The average age of ART initiation was 4.5 years (2 months - 180 months). Children under 5 years represented nearly one third (61.3%) of the sample.

The sex-ratio was 0.9 (47% male and 53% female).

The number of HIV infected children by the ART committee have increased from 2008 to 2010, decreased in 2011-2012 and increased again in 2013-2015. The year 2010 (51 out of 292, 17.5%) saw the higher number of patients.

The majority of patients (77.4%), were living in the health district of Tchaoudjo with Sokodé acting as the headquarter.

• Clinical findings

According to WHO classification, the clinical stages III (52.7%) and IV (20.3%) were the most frequent.

Wasting (40.1%), digestive candida infection (29.0%), acute respiratory infection (22.8%) and skin diseases (17.9%) were the main opportunistic affections. The HIV/tuberculosis co-infection has represented 6.7%.

• Biological indicators

The type 1 of VIH was found for all children (100%). Twenty one of them have had a PCR positive (under 18 months) (7.2%). The average rate of CD4 at the beginning of the ART was 552.98 ± 131.40 cell/mm³ (N = 241). A moderate to severe immunosuppression was observed (respectively 44.8% and 19.9%).

The pre-ART tests were in the norms (**Table 2**).

• Therapeutic approach

The First-line ART was essentially NEVIRAPINE + LAMIVUDINE + STAVUDINE (46.2%), then NEVIRAPINE + LAMIVUDINE + ZIDOVUDINE (27.7%) and LOPINAVIR-RITONAVIR + LAMIVUDINE + ABACAVIR (9.6%).

• Risk factors on ART

Factors associated with age were CD4 rate ($p < 0.0001$) and hemoglobin rate ($p < 0.0003$). Two factors (age and alanine aminotransferase rate) were associated with ART initiation using multivariate model. 0.13 represented the risk factor for initiating a protease inhibitor regime up to 2 years against under 2 years.

Table 2. Biological features of HIV infected children in the central, Togo.

BIOLOGICAL TEST	N	Average	DS
CD4 rate (cell/mm ³)	241	552.98	551.375
Creatinine rate (mg/L)	243	12.060	17.3059
Hemoglobin rate (g/dl)	235	10.978	10.0033
White cells account (cell/mm ³)	37	7643.77	4614.823
ALAT(UI/l)	274	46.33	

4. Discussion

• Epidemiologic estimates

Children represented only 5.1% of HIV infected patients. Many work streams confirm this situation in Sub-Saharan Africa: 5.8% in the Maritime Region in 2008 [5], 7% for the annual report of national AIDS care program [4], and 6% in Côte d'Ivoire [11] in 2016. The pediatric ART coverage in Togo (35%) remains low, despite increasing access to ART in general population [4]. The limited access to pediatric HIV testing is still a major barrier to improve the pediatric HIV treatment, e.g. shortage of PCR tests. Also, the significant neglect of PMTCT program, the lack of pediatricians, the quality of child care program integration and task shifting [4] are further hindrance. An important part of mothers are still not receiving PMTCT care, because antenatal care coverage is low (61.2%) in Togo and those who are attending private clinic without routine testing (34.0%) or delivering birth at home (50.5%) [12]. In 2012, only 13% of infants received PCR during their 6 - 8 first weeks [13].

The average age was 4.5 years. Late diagnosis and care are largely reported in African research paperwork: 4.42 years in Benin [14], 4.67 in Southern Togo [5] and 6.5% in Côte d'Ivoire [15]. In fact, in order to reduce the morbidity and death link to HIV infection on children, WHO had recommended since April 2008, an early viral diagnosis at the age of 6 weeks for exposed infant and rapid ART initiation [16]. This recommendation helps to strengthen the immunity system, reduce viral charge and the incidence of opportunistic disease. In our study, nearly two third of infected children (61.3%) were under five years old, as observed by other authors [5] [14] [17] [18]. This suggests that premature death and compromised survival rates to teenage are improved.

The female predominance (0.9% sex-ratio) are present in some of the literature [18] [19] [20] but not in others [6] [17] [21] [22]. In Togo, according to the Ministry of plan report in 2011, women represent 51% of the general population [7].

The HIV infected children were living mostly in district of Tchoudjo and the town of Sokodé (77.4%). Overall, in the wider population of Togo, the prevalence of HIV is higher in urban zones (3.5%) than in rural ones (1.6%) [3].

A reduction of new registrations has been observed from 2010 to 2014. The rapid depletion of rapid test (stock-out) appears to be the main cause. The second reason is the temporary suspension in 2011 of the clinical mentorship system, initiated in 2010 by the national AIDS program with Clinton Foundation support. This coaching conducted monthly by two regional pediatricians to support peripheral providers was known to strengthen child testing and improve clinical care [4]. So pediatric clinical mentorship should be strengthening in the Central Region of Togo.

• Clinical findings

According to WHO classification, the clinical stages III (52.7%) and IV (20.3%) were the most frequent. This late diagnosis on the children in the inves-

tigation was confirmed by the advanced stages (73.0% of pediatric AIDS). D'Almeida, Dicko-Traoré and Sagbo showed similar results, respectively of 52%, 92%, 93% and 65.2% [14] [17] [18] [19].

Wasting (40.1%), digestive candida infection (29.0%), acute respiratory infection (22.8%) and skin diseases (17.9%) were the most frequent opportunistic affections. Others authors found this morbidity, but in a different order: for example, D'almeida in Benin, buccal candida infection (71.9%) and wasting (60.9%) [17]. In Mali, wasting (73%) and pneumonia (45.9%) [18] [19].

Wasting constitutes the first opportunistic disease observed in our work. Those rates are lower than SAGBO's results (53.5%), but higher than OJUKWU results in Nigeria (33.8%) in 2007 [22] and DIARRASSOUBA ones (21.1%) in Côte d'Ivoire [15]. In Kenya in 2008, wasting was found on the 40% of inpatient infected children and led to up to half of morbidity link to AIDS disease on child [23]. Many reasons can explain the high prevalence of wasting among HIV infected children: insufficient food supply, anorexia, mouth ulceration, bad absorption, diarrhea or enteropathy due to HIV and the increase of metabolism link to opportunistic disease and HIV itself [24].

Acute respiratory infections are common opportunistic affections. The clinical signs and X-Ray were simple techniques used for the diagnosis. The germs responsible could not be isolated. Pneumonia was largely describe by others authors [25] [26] [27]. The pneumonia in pediatric HIV infection were often due to gram negative bacteria, *Pneumocystis jiroveci* and mycobacterium tuberculosis [28]. Bronchoalveolar lavage, required for the diagnosis of *Pneumocystis jiroveci* is not available in the Central Region of Togo.

Fungal infection as digestive candida is also observed as frequent HIV opportunistic affection among HIV infants: 19.8% for SAGBO [14] and 38.2% for OJUKWU [22]. In 2007, OJUKWU have identified buccal candida infection as a major factor for likelihood of HIV infection beyond 6 weeks of life. The digestive canal is one of the principal organs with an abundance of immuno-competent cells [26].

• Biological indicators

The type 1 of VIH was found for all children (100%). The type 1 of HIV was largely prevalent in West Africa. Its prevalence varies from 96% to 100% in Sub-Saharan countries [5] [11] [14] [18] [21]. One of the limit of our study was the absent of viral charge. This quantification had started since 2014 in Togo. In our work, clinical advanced stages are related to a severe immunodeficiency (44.8%), same as D'ALMEIDA results (56%) [17] in Benin, DIACK in Senegal [21] (57.1%) and SAGBO (74%) [19].

The average rate of hemoglobin (10.9 g/dl) was higher than the one in the Maritime Region (9.73 g/dl) [5], in the Southern part of Togo. In fact, wasting is known to be more prevalent in this southern region [3]. Anemia was found in the majority of HIV infected person with multifactor etiologies [29]. It is frequent in pediatrics population in Africa in general. In Togo and in Senegal, re-

spectively 70% and 85.6% of apparent healthy children have an anemia which originates from the iron deficiency [3] [30].

The remaining biological results were globally in the standard norms (creatinine, ALAT).

- **Therapeutic approach**

The first line regimen NEVIPARINE + LAMIVUDINE + STAVUDINE was the most prescribed ART combination (46.2%). Idem in the Maritime Region in Togo before 2011 (94.8%) [5] and in Benin before 2010 (90.5%) [14]. In fact, since 2010, WHO guidelines recommended replacing STAVUDINE by ZIDOVUDINE because of many side effects such as peripheral neuropathies. So the long period of our study extending from 2008 to 2015 explains the importance of NEVIPARINE+LAMIVUDINE+ZIDOVUDINE (27.7%) regimen. ART providers were not familiar with the regimen LOPINAVIR – RITONAVIR + LAMIVUDINE + ABACAVIR in the first line (9.6%), even though it had been recommended since 2010 with mothers receiving NEVIRAPINE in PMTCT services [9] [10].

- **Risk factors on ART**

Factors associated with age were CD4 rate ($p < 0.0001$) and hemoglobin rate ($p < 0.0003$). Two factors (age and alanine aminotransferase rate) were associated with ART initiation using multivariate model. 0.13 represented the risk factor for initiating a protease inhibitor regime up to 2 years against under 2 years. National guidelines recommend a protease inhibitor regime under 3 years because of the use of NEVIRAPINE in PMTCT program [9] [10]. According to alanine aminotransferase rate, the difference between ART regimes were not significant.

5. Conclusion

Pediatric HIV diagnosis remains delayed in the Central Region of Togo (average age for ART initiation 4.5 years) with advanced clinical stages (72.6%) and severe immunosuppression (44.8%). The initial ART was essentially NEVIRAPINE + LAMIVUDINE + STAVUDINE (46.2%). The achievement of UNAIDS 90-90-90 targets in 2020 appears hypothetical. However, a pediatric HIV national plan of acceleration has just been elaborated in March 2017. Strategies with high evidence as the early initiated diagnosis (EID), provider initiated testing and counselling (PITC) for each child attending health facilities and clinical mentorship have vigorously been strengthened. The key intervention should be the ART task shifting process started in 2015 in Togo.

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