



## Article Original

# Reporting of Five Years Mother to Child Transmission of HIV Among HIV-Exposed Infants Followed from 2009-2013 at “Centre Mère - Enfant” of the Chantal Biya Foundation (Yaounde)

*“Rapport sur cinq ans de transmission du VIH de la Mère à l'Enfant chez les nourrissons exposés au VIH suivis de 2009 à 2013 au Centre Mère et Enfant de la Fondation Chantal Biya à Yaoundé, Cameroun”*

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### ABSTRACT

**Introduction.** Pediatric HIV infection is still a Public Health issue in developing Countries. Survival of HIV-infected children is closely related to early combined antiretroviral therapy (cART). Thus, it is very important to improve access to Prevention of Mother To Child Transmission of HIV (PMTCT), diagnosis and care. The aim of this paper is to describe rates of HIV transmission among HIV exposed infants followed in an outpatient clinic. **Methods.** Analysis of routine data collected from 2009 to 2013 has been conducted in the “Centre Mère et Enfant” in Yaoundé, Cameroon. All HIV-exposed infants coming for their first consultation in the clinic during these 5 years have been registered. HIV PCR diagnosis until one year and HIV serology beyond were offered free of charge. **Results.** As a whole, among the 2,768 HIV-exposed infants, 2068 children were HIV-uninfected (1 death, 1150 uncompleted follow-up), 322 were HIV-infected (19 deaths, 8 uncompleted follow-up) and 378 were not tested for HIV status or with no result available (23 deaths). Mean follow-up=260 days. 1,434 boys and 1,334 girls. When mother and/or child received any ART treatment, the transmission rate of HIV was 5.64% when transmission rate was of 43.6% when mother and child received nothing as a treatment. The main factor in relation with low rate of transmission was any treatment in mother or baby. Two other factors of lower transmission were artificial feeding, and PMTCT in reference hospitals. **Conclusion.** In a routine program, as expected, percentage of HIV infected children is much more important among children or mothers who did not have access to PMTCT or ART treatment. In the context of elimination of Mother to Child transmission of HIV access to HIV testing and PMTCT must be increased, especially in private and small health centers

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### RÉSUMÉ

**Introduction.** L'infection à VIH pédiatrique demeure un problème de santé publique dans les pays en développement. La survie des nourrissons infectés par le VIH dépend étroitement de l'initiation précoce du traitement antirétroviral. Nous décrivons la transmission du VIH chez les nourrissons exposés au VIH suivis dans un hôpital de référence à Yaoundé. **Matériels et méthodes.** Les données de routine recueillies dans une cohorte de nourrissons exposés au VIH de 2009 à 2013 au Centre Mère et Enfant de Yaoundé ont été analysées. **Résultats.** Parmi 2768 nourrissons exposés au VIH, 2068 nourrissons n'étaient pas infectés par le VIH (1 décès, 1150 suivis inachevés), 322 étaient infectés par le VIH (19 décès, 8 suivis inachevés) et 378 n'étaient pas testés ou ne disposaient pas de résultat de test du VIH (23 décès). La transmission du VIH était de 5,64 % en cas d'une notion de traitement antirétroviral chez la mère ou l'enfant et de 43,6 % dans le cas contraire. Les facteurs associés à une faible transmission du VIH étaient la notion de traitement antirétroviral chez la mère ou le nourrisson, l'alimentation artificielle et le suivi prénatal dans un hôpital de référence. **Conclusion.** En routine, la transmission du VIH parmi les nourrissons exposés au VIH est plus importante en cas de manque d'accès à la PTME ou au traitement antirétroviral. Cet accès doit être renforcé dans les formations sanitaires de catégorie inférieure ou privées afin d'éliminer la transmission du VIH de la mère à l'enfant.

## INTRODUCTION

Prevention of mother to child transmission of HIV is now known for 20 years (1). In western countries, pediatric HIV infection has been eradicated in the last years of 20th century (2). Many studies have been conducted in developing countries (3-6) and WHO has published recommendations for PMTCT several times between 2006 and 2015 (7-9). In some African countries, elimination of MTCT is now achievable due to testing for HIV and managing HIV infection in more than 80% of pregnant women (10). However, the percentage of pregnant women tested for HIV remain below 50% in many other African countries and we need more information to improve implementation of PMTCT programs (10).

In each country where PMTCT should be improved, the situation must be analyzed first at site level to better understand why it does not work properly.

This cohort study aimed at describing the proportion of HIV-infected infants among HIV-exposed infants received routinely in a reference center in Yaoundé, Cameroon, beyond research studies and pilot sites, and to identify factors associated to mother to child transmission of HIV in the routine follow-up.

## METHODS

### Study design and procedures

We analyzed the medical files of all HIV-exposed infants received from 2009 to 2013 in the Day Care Unit of « Centre Mère et Enfant de la Fondation Chantal Biya », one of the reference health facilities, pioneer in PMTCT and paediatric HIV activities in Cameroon. HIV-Exposed children were planned according to National guidelines to be seen at health facilities at 6, 10, and 14 weeks coinciding with the EPI calendar, then 6, 9, 12 and 15 months. The early infant diagnosis (EID) using PCR was proposed from 6 weeks of age and the serology from 12 months of age. If the first HIV test is positive, a second sample was taken for confirmation. If the first test was negative in breastfeeding child, a second test was planned 6 weeks after weaning.

All HIV-exposed infants seen at least once in the clinic were routinely registered in a medical file. This file was then computerized. The HIV diagnosis (virological or serological) was performed free of charge from six weeks to 15 months of age. The medical files were updated for HIV diagnosis on a regular basis.

### Outcome

Infants were classified according to HIV status as following: 1) HIV-infected with at least one positive HIV PCR (from six weeks of age) or a positive serology when older than 15 months, 2) HIV-uninfected with at least one negative HIV PCR or negative HIV serology beyond 15 months of age after breastfeeding has been stopped, 3) Not tested or no result available when the HIV PCR or HIV serology have not been performed or when results have not been displayed.

We also classified infants according to follow-up delay as: 1) alive and followed when the last visit for HIV-uninfected infants was beyond 359 days or when HIV-

infected infants have been started with combined antiretroviral treatment (cART), 2) lost to follow-up for all HIV-uninfected infants never seen after the last visit before age 12 months ??, according to national recommendations.

### Sample collection and HIV diagnosis in the laboratory

At contact visit with HIV-exposed infants attending the « Centre Mère et Enfant de la Fondation Chantal Biya » in Yaounde, whole blood was collected into EDTA-containing anticoagulant tubes and transferred to the Virology Laboratory of Centre Pasteur of Cameroon for children included in the ANRS-Pediacam study. Samples from children not part of the above mentioned study were collected onto filter papers (DBS), processed according to standard procedures and transported to the National Program Reference laboratory at the CIRCB. Two types of biological methods were used to test samples for HIV using PCR. When children were enrolled in the Pediacam cohort study, HIV PCR was done with Generic HIV Charge virale™ (Biocentric). When children were in the routine follow-up, the HIV PCR was performed with Roche™ kits. In both cases, the HIV serological test was done by Determine HIV1/2™ (Abbot Diagnostics) with Oraquick™ (OraSure Technologies Inc, Bethlhem, PA, USA) as confirmation test.

### Variables and statistical analysis

We considered three methods of infant feeding at baseline: bottle feeding, exclusive breastfeeding and mixed feeding.

Mothers were classified in three groups based on the used or not of any antiretroviral therapy: none, highly active antiretroviral therapy (HAART) and PMTCT prophylaxis (whatever was the prophylaxis). For children, two groups were considered: none or any antiretroviral drug. We also performed an analysis with two modalities: none versus any antiretroviral drug in mother and in infant.

We categorized place where antenatal care was conducted in four modalities: none, private clinics or health centers, district hospitals and reference hospitals.

The fact that some infants have been enrolled in a cohort study since birth: Pediacam (ANRS 12140) (11) was also considered.

Data were analyzed with Stata™. We performed a multivariate logistic regression including factors with a p-value <0.2 and factors available in database and potentially associated with HIV transmission from mother to child: age of the mother, sex, year of coming, clinical trial, matrimonial status, site of PMTCT, number of antenatal visits, site of delivery, low birth weight, infant feeding, malaria prophylaxis, and any antiretroviral treatment in mother or child.

### Ethical considerations

This study was conducted after getting ethical clearance from the Cameroon National Committee of Ethics and administrative authorization from the Ministry of Public Health.

## RESULTS

### Study population

A total of 2768 HIV-exposed infants were seen for the first time in the day care unit from 2009 to 2013 at a median age of 50 days, of whom 1434 (51.8%) were male (Table 1). Six hundred and fourteen (22%) infants were enrolled in the ANRS-12140 PEDIACAM cohort study. One hundred and thirty-nine (5.0%) mothers had not received any antenatal care while 696 (25.2%), 532 (19.2%) and 1400 (50.6%) have carried out antenatal care respectively in a health center or private hospital, a district hospital and a reference hospital. Prior to the first visit, 2311 (83.5%) infants had been exposed to the antiretroviral drug directly or indirectly (antiretroviral drug in the mother) as a mean of protection. Respectively 1831 (67.0%), 756 (27.7%) and 145 (5.3%) mothers were carrying out artificial feeding, exclusive breastfeeding and mixed feeding up to the first visit. By the end of study follow-up, 43 (1.6%) infants had died, 1726 (62.4%) were lost to follow-up and 999 (36.1%) were followed properly. Further, the HIV status of 378 (13.7%) infants was indeterminate while 322 (11.6%) and 2068 (74.7%) infants were HIV-infected and HIV-uninfected respectively.

We describe in table 1 the main characteristics of the 2,768 HIV exposed children seen in the clinic from 2009 to 2013.

### Factors associated with mother to child transmission of HIV

When considering mother to child transmission of HIV according to any ART treatment received by the mother and/or child, we observed a transmission rate of 5.64% (Table 2). When neither the mother nor the infant received anything as Prevention of mother to child transmission of HIV (PMTCT), the transmission rate of HIV was of 43.6%.

Respectively 4.1%, 8.9% and 43.6% infants were infected when the mother received HAART, antiretroviral prophylaxis and no prophylaxis. This difference was statistically highly significant ( $p < 0.001$ ).

The transmission of HIV infection was significantly higher among infants who were mixed fed or breastfed than in those who were artificially fed, respectively 56.89%, 25.34% and 5.43% ( $p < 0.001$ ). But when considering treatment received by women according to infant feeding, we observed that there were only 21.5% of mixed feeding mothers and 44.4% of breastfeeding mothers receiving HAART during pregnancy in contrast with 60.9% among mothers who artificially fed.

The main factor, in multivariate analysis, in relation with low rate of transmission is any treatment in mother or baby. Two other factors of lower transmission were artificial feeding, and PMTCT in reference hospitals (Table 2).

## DISCUSSION

The main result of our study shows that in routine conditions of follow-up, when mother or child receive any antiretroviral treatment, rate of transmission is 5.64% in contrast with rate of transmission of 43.6% when they

received nothing as PMTCT. It means that even in routine conditions, a low rate of mother to child transmission of HIV can be achieved in Yaoundé on a long period of time. The rate of indeterminate results of HIV test in infants was very high: 13.7% of 2768 HIV exposed children, of whom two third were too young to obtain their final status. More importantly, 1726 children were considered as lost to follow-up. However, their HIV status was known by health care providers while some mothers did not come back to the health facility when the child was aged from 15 months to age 18 months in order to retry the last HIV test result. Anyway, this high rate shows the poor quality of follow-up in a routine health structure. These two results show clearly the difficulties of implementing a PMTCT program in many structures.

Rates of transmission are much higher among breastfeeding mothers than among mothers who chose artificial feeding. In fact, choosing artificial feeding is like a surrogate marker of antiretroviral treatment in our study. Indeed artificial feeding is largely used by mothers and caregivers as shown in another analysis of this database (12). The percentage of mothers with exclusive breastfeeding is less than 20% and for an average duration of three months.

The rate of HIV transmission among exposed children without any PMTCT is higher among children whose mothers came late in this outpatient clinic, representing around 10% of the mothers, as shown in a previous study (13). A fact which is important to consider is that we are comprehensive in this study. All exposed children during 5 consecutive years were enrolled in this database.

Anyway, this study took place in one of the reference sites for PMTCT in Cameroon. Therefore, in other health structures, rates of HIV transmission could be higher as shown in the multivariate analysis. Another risk factor of transmission is having been followed in another health facility than a reference hospital. Thus, we should advocate for reinforcement of PMTCT in private and peripheral health structures.

Contrary to a South African study (14), the young age of mothers was not a risk factor for MTCT of HIV in our study.

## CONCLUSION

Rate of mother to child transmission of HIV in a routine program can be low when mothers and children have access to antiretroviral therapies. Access to HIV testing and care for HIV infected pregnant women should be reinforced particularly in health centers and private clinics. A better health system organization has to be considered in order to reduce rate of lost-to-follow among HIV exposed children.

## DECLARATIONS

### Competing interests

The authors declare that they have no competing interests.

### Funding

There was no funding for this study.

**Authors' contributions**

**ANF** participated in the study design and conception, the recruitment and follow up of HIV-infected infants, the data analysis, the manuscript writing and the study coordination.

**NJA** participated the recruitment and follow up of HIV-infected infants, the manuscript writing and the study coordination.

**TM** participated in the study design and conception, the manuscript writing and the study coordination.

**KC** participated in the recruitment and follow up of HIV-infected infants and the manuscript writing.

**KP** participated in the manuscript writing and the study coordination.

**PM** participated in the study design and conception, the data analysis, the manuscript writing and the study coordination.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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**Table 1: Main characteristics of HIV exposed children from 2009 to 2013, Day Care Unit « Centre Mère et Enfant de la Fondation Chantal Biya » Yaounde Cameroon**

| Variable  | n    | (%) or median (IQR) |
|---|------|---------------------|
| <b>Calendar year</b>  |      |                     |
| 2009  | 558  | (20.2)              |
| 2010  | 495  | (17.9)              |
| 2011  | 501  | (18.1)              |
| 2012  | 619  | (22.4)              |
| 2013  | 595  | (21.5)              |
| <b>Sex</b>  |      |                     |
| Male  | 1434 | (51.8)              |
| Female  | 1334 | (48.2)              |
| <b>Enrolled in ANRS-12140 Pediacam cohort study</b>   |      |                     |
| Yes   | 614  | (22.0)              |
| No  | 2154 | (78.0)              |
| <b>HIV status</b>   |      |                     |
| Uninfected  | 2068 | (74.7)              |
| Infected  | 322  | (11.6)              |
| Indeterminate   | 375  | (13.7)              |
| <b>Mother age (N), median (IQR)</b>   | 2656 | 30 (26 – 33)        |
| <b>Father age (N), median (IQR)</b>   | 2451 | 36 (24 – 41)        |
| <b>Outcome</b>  |      |                     |
| Followed properly   | 999  | (36.1)              |
| Lost to follow up   | 1726 | (62.4)              |
| Dead  | 43   | (1.6)               |
| <b>Any antiretroviral drug in baby (including ARV in mother)</b>  |      |                     |
| Yes   | 2311 | (83.6)              |
| No  | 457  | (16.5)              |
| <b>Antiretroviral drug in mother</b>  |      |                     |
| HAART   | 1423 | (51.4)              |
| Prophylaxis in mother (alone or with the baby)  | 693  | (25.0)              |
| None  | 652  | (23.6)              |
| <b>Site of antenatal care (N=2,764)</b>   |      |                     |
| None  | 139  | (5.0)               |
| Health center or private clinic   | 696  | (25.2)              |
| District hospital   | 532  | (19.2)              |
| Reference Hospital  | 1400 | (50.6)              |
| <b>Method of feeding (N=2,732)</b>  |      |                     |
| Artificial feeding  | 1831 | (67.0)              |
| Exclusive breastfeeding   | 756  | (27.7)              |
| Mixed feeding   | 145  | (5.3)               |
| <b>Birth weight (N=2,534)</b>   |      |                     |
| <2,500 g  | 375  | (14.8)              |
| ≥2,500 g  | 2159 | (85.2)              |
| <b>n: Size of the study population; %: Percentage; IQR: Interquartile range; N: Total number of entities considered; HAART: Highly active antiretroviral treatment.</b> |      |                     |