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Research Article

Reporting of Five Years Mother to Child Transmission of HIV among HIV-Exposed Infants Followed from 2009-2013 in the "Centre et Mère et Enfant de Yaoundé", Chantal Biya Foundation, Cameroon

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Abstract

Introduction: Paediatric Human Immunodeficiency Virus (HIV) infection remains 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. This study at assessing Mother to Child Transmission of HIV (MTCT) and to identify factors associated with MTCT in infants born of HIV-infected mothers and routinely followed in referral pediatric hospital in Yaounde, Cameroon.

Methods: In this cohort study, we included all the HIV-exposed infants who attended at least once the Day Care Unit of the "Centre Mère et Enfant de Yaoundé", Chantal Biya Foundation, Cameroon, from 2009 to 2013. The Early Infant Diagnosis of HIV (EID) using Polymerase Chain Reaction (PCR) was proposed from the age of 6 weeks, and the HIV serology was conducted from the age of 12 months. HIV-exposed infants were classified according to HIV status as following: 1) HIV-infected infants, 2) HIV-uninfected infants, 3) infants not tested or with no HIV test result available. Association between the HIV status outcome and the exposure variables was assessed using multivariate logistic regression, including factors with a p-value < 0.20 in univariate analysis and other potential risk factors of MTCT. Infants with indeterminate HIV status were excluded both in univariate and multivariate analysis.

Results: Of 2,768 HIV-exposed infants, 2068 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 the mother and/or the infant received any antiretroviral treatment, MTCT was 5.64% versus 43.6% when mother and child received nothing as a treatment. The main factor associated with lower MTCT was history of any antiretroviral treatment in HIV-infected mother or HIV-exposed infant. Artificial feeding and antenatal monitoring of HIV-infected mother in a referral hospital were also associated with lower MTCT.

Conclusion: In a routine program, as expected, MTCT is much more important among HIV-exposed infants or mothers who did not have access to antiretroviral drugs for PMTCT. Moreover, access to HIV testing and PMTCT must be increased, especially in private and peripheral level health facilities.

Keywords: Child Transmission; HIV; PMTCT

Introduction

Globally, more than 90 percent of new pediatric Human Immunodeficiency Virus (HIV) infections are in sub-Saharan Africa [1]. Mother-to-child transmission (MTCT) is the most common mean of acquiring pediatric HIV infection since more than 90% of new HIV infections among children are through mother-to-child transmission. Without any intervention measures to prevent the transmission, the risk of MTCT ranges from 20% to 40%. However, MTCT can be reduced to less than 2% in non-breastfeeding populations. In breast feeding populations, the transmission can be reduced less than 5% with effective interventions during the periods of pregnancy, labor, delivery and breastfeeding [2]. Prevention of mother-to-child transmission (PMTCT) is one of the fundamental approaches to control HIV epidemic [1,3].

In developed countries, MTCT has been quite eradicated in the last years of 20th century due to several interventions [4]. Following these successes, the World Health Organization (WHO) has updated recommendations in regard with PMTCT several times between 2006 and 2015 [5,6]. However, the path toward progress has been slower in sub-Saharan Africa because of limited health infrastructure and high disease burden. The proportion of pregnant women tested for HIV remains below 50% in many sub-Saharan African countries and there is a need of more information to improve implementation of PMTCT programs [6]. This situation that needs to be understood properly could be examined at the site level. This study aimed at assessing MTCT and to identify factors associated with MTCT in infants born of HIV-infected mothers and routinely followed in referral pediatric hospital in Yaounde, Cameroon: the "Centre Mère et Enfant de Yaoundé", Chantal Biya Foundation, Cameroon.

Methods

Study design and procedures

We analyzed the medical files of all HIV-exposed infants followed from 2009 to 2013 in the Day Care Unit of the « Centre Mère et Enfant de la Fondation Chantal Biya », Yaounde, Cameroon. This site is one of the referral health facilities, pionneer in PMTCT and pediatric HIV care in Cameroon. HIV-Exposed children were followed according to national guidelines, at 6, 10, and 14 weeks, modeled on the Enlarged Program Immunization (EPI) schedule, and then at 6, 9, 12 and 15 months. The Early Infant Diagnosis of HIV (EID) using Polymerase Chain Reaction (PCR) was proposed from the age of 6 weeks, and the HIV serology was conducted from the age of 12 months. If the first EID was positive, a second blood sample was taken for a confirmation EID. However, if the first EID was negative in a breastfed infant, a second EID was conducted 6 weeks after weaning. The HIV diagnosis test (EID or serology) was performed free of charge from six weeks to 15 months of age.

All HIV-exposed infants seen at least once in the Day Care Unit were routinely registered in medical files. The medical files data were entered into an electronic database and updated for HIV diagnosis on a regular basis.

Blood samples collection and HIV diagnosis in the laboratory

During the first attendance visit of HIV-exposed infants in the « Centre Mère et Enfant de la Fondation Chantal Biya » in Yaounde, whole blood was collected into Ethylenediaminetetraacetic (EDTA)-containing anticoagulant tubes and transferred to the "Centre Pasteur of Cameroon (CPC)" laboratory, Yaounde, for those who were enrolled in the ANRS-Pediacam cohort study [7,8]. For the other ones, blood samples were collected Dry Blood Spots (DBS) and transported to the "Centre international de Référence Chantal Biya (CIRCB)" laboratory, Yaounde. Blood samples were tested for HIV using one of the two following PCR method: Generic HIV Charge virale™ (Biocentric) in the CPC laboratory or Roche™ kits in the CIRCB laboratory. In both cases, the HIV serological test was conducted using Rapid Diagnostic Tests with Determine HIV1/2™ (Abbot Diagnostics) as the first test and Oraquick™ (OraSure Technologies Inc, Bethlhem, PA, USA) as confirmation test (if the first test was reactive).

Outcomes

HIV-exposed infants were classified according to HIV status as following: 1) HIV-infected infants with at least one positive EID (from the age of 6 weeks) or a positive HIV serology in infants older than 18 months, 2) HIV-uninfected infants with at least one negative EID or negative HIV serology beyond the age of 18 months, after breastfeeding has been stopped, 3) infants not tested or with no HIV test result available. They were also distinguished according to follow-up outcome as: 1) alive and followed for HIV-uninfected infants followed beyond the age of 12 months or HIV-infected infants started on combined antiretroviral therapy (cART), 2) lost to follow-up for HIV-uninfected infants whose follow-up was abandoned before the age of 12 months, 3) dead for any infant who died before the age of 15 months.

Exposure variables

The three methods of infant feeding considered at baseline were: 1) artificial feeding, 2) exclusive breastfeeding and 3) mixed feeding.

The HIV-infected mothers were classified in three groups according to their status in relation antiretroviral prophylaxis as: 1) none, 2) Highly Active Antiretroviral Therapy (HAART) or 3) PMTCT prophylaxis. The HIV-exposed infants were also classified according to their status in regard with antiretroviral prophylaxis as 1) none versus 2) any antiretroviral drug in mother and in infant. The Cameroonian guidelines recommended two approaches (also called "options") for PMTCT prophylaxis. With "Option A," pregnant women were to start zidovudine (ZDV) monotherapy during the antenatal period and, around delivery, take a single-dose of nevirapine (NVP) with a week-long "tail" of zidovudine-lamivudine (ZDV-3TC). HIV-exposed infants were prescribed continuous daily nevirapine (NVP) from birth until the cessation of breastfeeding. In the "Option B" strategy, women not yet eligible for ART were to initiate three-drug combination antiretroviral prophylaxis during the antenatal period and continue until the cessation of breastfeeding. During the first six weeks of life, their HIV-exposed newborns were to receive daily nevirapine (NVP) prophylaxis.

The site of antenatal care was categorized in four modalities as: 1) none, 2) private health facility, 3) district hospital or, 4) reference hospital.

History of HIV-exposed infant's enrollement in the 12140 ANRS-Pediacam cohort study [7,8] was also considered.

The other exposure variables considered were: marital status of mother, number of antenatal visits, site of delivery, infant sex, infant birth weight, calendar year of enrolment of infant in PMTCT care, malaria prophylaxis.

Statistical analysis

The association between the HIV status outcome and the exposure variables was assessed using multivariate logistic regression, including factors with a p-value <0.20 in univariate analysis and other potential risk factors of MTCT. Infants with indeterminate HIV status were excluded both in univariate and multivariate analysis.

Data were analyzed using Stata™.

Results

Study population

In all, 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 respectively 696 (25.2%), 532 (19.2%) and 1400 (50.6%) have carried out antenatal care 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, respectively 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 respectively 322 (11.6%) and 2068 (74.7%) infants were HIV-infected and HIV-uninfected.

We described in table 1 the main characteristics of the 2,768 HIV-exposed infants seen in the Day Care Unit from 2009 to 2013.

Factors associated with mother to child transmission of HIV

In univariate analysis, MTCT estimate was respectively 5.64% and 43.6% in when there was history of antiretroviral treatment in the HIV-infected mother or HIV-exposed infant, and when neither the HIV-infected mother nor the HIV-exposed infant received anything as PMTCT prophylaxis (Table 2). 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 significant ($p < 0.001$). MTCT was significantly higher among HIV-exposed infants who were mixed fed (56.89%) or breastfed (25.34%), compared to those who were artificially fed (5.43%), ($p < 0.001$).

In multivariate analysis, the main factor associated with lower MTCT was history of any antiretroviral treatment in the HIV-infected mother or HIV-exposed infant. Two other factors associated with lower MTCT were artificial feeding, and antenatal monitoring of the HIV-infected mother in a referral hospital (Table 2).

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

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.

n: Size of the study population; %: Percentage; IQR: Interquartile range; N: Total number of entities considered; HAART: Highly active antiretroviral treatment.

Variable	Univariate analysis		Multivariate analysis	
	Infant HIV status N = 2390			
	HIV-uninfected n = 2068	HIV-infected n = 322	P-value 1	p-value 2
Calendar year			0.157	0.400
2009	457	58		
2010	382	62		
2011	353	69		
2012	447	75		
2013	429	58		
Sex			0.794	0.780
Male	1,063	163		
Female	1,005	159		
Infant enrolled in ANRS-12140 Pediacam cohort study			0.056	0.450
Yes	526	66		
No	1,542	256		
Outcome of infant follow-up*			<0.001	
Followed properly	872	116		
Lost to follow-up	1,195	187		
Dead	1	19		
Mother status in relation with ART			<0.001	<0.001
HAART	1,238	53		
ARV prophylaxis	552	54		
None	278	215		
History of ARV drug in infant or mother			<0.001	<0.001
Yes	1,790	107		
No	278	215		
Site of antenatal care			<0.001	<0.001
None	64	44		
Private health facility or health center	419	142		
District hospital	361	88		
Referral hospital	1,221	48		
Method of infant feeding			<0.001	<0.001
Artificial feeding	1,519	87		
Exclusive breastfeeding	483	164		
Mixed feeding	50	66		
Birthweight			0.161	0.420
< 2,500g	266	44		
≥ 2500g	1,690	218		

Table 2: Factors associated with MTCT in HIV-exposed infants from 2009 to 2013 in the Day Care Unit, "Centre Mère et Enfant de la Fondation Chantal Biya", Yaounde, Cameroon.

p-value 1: Chi-square test; p-value 2: Wald test; ANRS: "Agence Nationale de Recherches sur le SIDA et les Hépatites" – French National Agency of Research on HIV and Hepatitis; *: Variable not included in multivariate analysis because of a very small size of one category; ART: Antiretroviral therapy; HAART: Highly active antiretroviral therapy; ARV: antiretroviral*Antiretroviral treatment.

Discussion

The main result of our study showed that in routine conditions of follow-up, when HIV-infected mothers or HIV-exposed infants receive any antiretroviral treatment, MTCT is 5.64% in contrast with the proportion of 43.6% HIV-infected infants when they received nothing as PMTCT. This result was similar to that reported in previous cohort studies conducted in other countries where successful PMTCT interventions have been carried out [4,9-12].

The proportion of indeterminate results of HIV test (13.7%) in HIV-exposed infants was quite high. Noteworthy, 1726 from a total of 2768 infants were considered as lost to follow-up after the age of 15 months while their HIV test result was available in the Day Care Unit but not withdrawn by the mothers. This situation clearly showed poor quality of routine follow-up of HIV-exposed infants and difficulties in implementing a PMTCT program in many Cameroonian health facilities. As demonstrated in other sub-Saharan countries, although PMTCT programs are widely implemented, many HIV-exposed infants fail to benefit because of lost to follow up [13-15], which leads to delays or no initiation of interventions, thereby contributing to significant child morbidity and mortality.

MTCT was 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 was largely practiced by mothers and caregivers as shown in another analysis of this database [16]. The proportion of mothers with exclusive breastfeeding was less than 20% and for an average duration of three months.

MTCT among HIV-exposed infants without any PMTCT was higher among those whose mothers started antenatal care later, representing around 10% of the mothers, as shown in a previous study [17]. Antenatal monitoring of mothers in Health facilities other than referral hospital was also associated with MTCT, stressing the need to reinforce in private and peripheral level health facilities.

Conclusion

Mother to child transmission of HIV (MTCT) in a routine program could be low when HIV-infected mothers and their infants get early access to antiretroviral drugs for Prevention of Mother to Child Transmission of HIV (PMTCT). Access to HIV testing and care to HIV- infected pregnant women should be reinforced particularly in in private and peripheral level health facilities. A better health system organization has to be considered in order to reduce lost-to-follow among HIV-exposed infants.

Ethics Approval and Consent to Participate

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

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