



ORIGINAL ARTICLE

PCR Results and PMTCT Treatment Outcomes among HIV-Exposed Infants in a Tertiary Hospital in Nigeria, 2010-2014

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ABSTRACT

Background: Early infant diagnosis (EID) of human immunodeficiency virus (HIV) infection in pediatrics with the use of DNA polymerase chain reaction (PCR) is a way of assessing the retroviral status of HIV-exposed infant with the view of early commencement of treatment for infected infants. It also serves as a way of assessing the effectiveness of prevention of mother-to-child transmission of HIV (PMTCT) in health care facilities.

Methods: This was a 5-year prospective cross-sectional study at the Ekiti State University Teaching Hospital, (EkSUTH) Ado-Ekiti, Nigeria. Babies delivered to HIV-positive mothers who presented at EkSUTH between January 2010 and December 2014 were enrolled in the present study. PCR was done twice for all HIV-exposed infants. Statistical analysis was done using SPSS version 16.0.

Results: One hundred and fifty eight infants were HIV exposed; 72 males and 86 females (M:F= 0.84:1). Eighty eight (55.7%) of the mothers had commenced highly active anti-retroviral therapy (HAART) before pregnancy, 56 (35.4%) during pregnancy, and 14 (8.9%) after delivery. Ten (6.3%) babies tested positive. Four (28.6%) of 14 exposed babies whose mothers commenced HAART after delivery tested positive to HIV compared to 3 (5.4%) of 56 babies whose mother commenced HAART during pregnancy and 3 (3.4%) of 88 babies whose mother commenced HAART before pregnancy. The difference was statistically significant ($\chi^2 = 13.28$, $df = 4$, $p = 0.01$).

Conclusions and Global Health Implications: There is significant reduction in transmission of HIV from mothers to children with commencement of antiretroviral drugs before pregnancy in mothers and use of Nevirapine for all exposed babies for the first 6 weeks of life. Infants of HIV positive mothers can live healthy life free of HIV infection if their mothers participate in PMTCT program.

Key words: HIV • PCR • Infants • Treatment Outcomes • PMTCT • Nigeria

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Introduction

HIV/AIDS is still a disease of public health importance and mother to child transmission (MTCT) is one of the major routes of spread of the virus.^[1] About 330,000 children under the age of 15 became infected with HIV in the year 2012 worldwide according to recent estimates by the Joint United Nations Program (UNAIDS) on HIV/AIDS with more than 90 percent of paediatric HIV infections occurring in sub-Saharan African countries.^[1] Most of these infections occurred during pregnancy, delivery or breastfeeding thereby making the prevention of mother to child transmission (PMTCT) a major public health approach of reducing the scourge.^[2] Efforts have been made over the past few years to improve PMTCT in some sub-Sahara African countries.^[3-5] One of the major ways of reducing the scourge of HIV/AIDS is by ensuring early infant diagnosis (EID). The World Health Organization (WHO) recommends that infants of HIV positive mothers should have polymerase chain reaction (PCR) done between 4 to 6 weeks of life for early infant diagnosis and commencement of antiretroviral therapy in HIV positive infants below 24 months of age.^[1-3] Nigeria has about 3 million people living with HIV and the prevalence of HIV infection among pregnant women attending antenatal clinic (ANC) is about 4.4% with mother-to-child transmission of HIV occurring in about 10% of these.^[4,6] Despite sustained effort at preventing mother to child transmission of HIV, infant of HIV positive mothers are still at risk of becoming infected, especially in developing countries where resources for patients' care are limited.^[7-9] In the year 2010, new pediatric HIV infection was estimated at 390,000 globally and only 23% of HIV infected children have access to antiretroviral drugs.^[8,10] Data from previous studies show that only 10-12% of HIV-exposed infants have access to EID.^[7,8,10,11] EID reported in this study commenced in the Pediatrics department of EkSUTH in 2009, though the samples were analyzed at Obafemi Awolowo University Teaching Hospital, (OAUTH) Osun State, Nigeria. The purpose of this study was to assess HIV reactivity rate among HIV- exposed infants seen in the Pediatrics department of EkSUTH over a five year period.

Methodology

This was a prospective cross sectional study carried out at the Pediatric ART clinic of EkSUTH, Ado-Ekiti from January 2010 to December 2014. Dried blood spot (DBS) samples, taken at six weeks of life and two weeks after discontinuation of breastfeeding at one year of life, from infants of HIV positive mothers who were delivered within and outside EkSUTH were transported by courier to OAUTH, Ile-Ife, Osun State, Nigeria (about 2 hours drive from Ado-Ekiti) for analysis. EkSUTH is a relatively new teaching hospital (upgraded from a specialist hospital to a teaching hospital in the year 2008). EID commenced in the center in 2009 and since then DBS samples for DNA PCR collected in EkSUTH were analyzed in OAUTH, Osun State, Nigeria which is the regional head area for PCR analysis for Institute of Human Virology, Nigeria (IHVN).^[9,12] IHVN provides support for training of health workers in treatment of HIV patients in Nigeria.^[12] Results usually become available in about two months from the time of sample collection. The PCR analysis was carried out using the GeneAmp PCR System 9700 (Perkin-Elmer, Norwalk, Conn, USA). PCR analysis of HIV-exposed infants was an ethically built-in program into the approved PMTCT services in EkSUTH. Statistical analysis was done with SPSS version 16 for Windows (SPSS Inc, Chicago, USA) after data was manually sorted and entered. The DNA PCR result of the HIV-exposed infants was categorized into positive and negative. This was cross-tabulated with the time mothers commenced HAART in pregnancy, feeding method, and the time babies commenced Nevirapine after delivery. Differences in proportion were tested with chi square and *p* value less than 0.05 was regarded as significant.

Results

One hundred and fifty eight HIV-exposed infants did DNA PCR test during the study period and this comprised of 72 males and 86 females giving a male to female ratio of 0.84:1 (Table I). One hundred and twenty four (78.5%) babies were delivered in government hospitals, 23 (14.6%) in private hospitals, 7 (4.4%) in faith-based homes and the remaining 4 (2.5%) at home (Table I). Delivery was

Table I. Selected Characteristics of 158 Infants of HIV Positive Mothers Seen at Ekiti State University Teaching Hospital (EKSUTH), Nigeria

Characteristics of HIV- exposed Infants (N=158)	Frequency	Percent
Sex		
Male	72	46.7
Female	86	53.3
Place of delivery		
Government Hospital	124	78.5
Private Hospital	23	14.6
Faith based centre	7	4.4
Home	4	2.5
Mode of delivery		
Vaginal	144	91.1
Caesarean section	14	8.9
Timing of mother haart commencement		
Before pregnancy	88	55.7
During pregnancy	56	35.4
After delivery	14	8.9
Feeding option adopted by mother		
Exclusive breastfeeding	142	89.9
Breast milk substitute	13	8.2
Mixed feeding	3	1.9
Outcome		
HIV negative	148	93.7
HIV positive	10	6.3
HIV positivity outcome by feeding methods		
Exclusive breastfeeding (n=142)	9	6.3
Breast milk substitutes (n=13)	1	7.7
Mixed feeding (n=3)	0	0.0

by Caesarean section in 14 (8.9%) and per vaginal in 144 (91.1%). HIV status of the babies' fathers was positive in 4 (2.5%), negative in 63 (39.9%), and unknown in 91 (57.6%). One hundred and forty two (89.9%) babies had exclusive breast feeding, 13 (8.2%) had breast milk substitute and 3 (1.9%) had mixed feeding. Eighty-eight (55.7%) mothers commenced HAART before pregnancy, 56 (35.4%) during pregnancy, and 14 (8.9%) after delivery (Table I). Nevirapine was given for the first 6 weeks of life in 147 (93.0%) of the babies while the remaining 11 (7.0%) did not receive Nevirapine. Six (54.5%)

of the 11 exposed babies who did not receive Nevirapine tested positive to HIV compared to four (2.7%) of the 147 exposed babies who received Nevirapine for the first 6 weeks week of life. The difference is statistically significant ($\chi^2 = 47.089$, $df = 1$, $p = <0.001$). There was no significant difference with regards to HIV positivity vis-à-vis mode of delivery as nine (90%) of the ten babies who tested positive were delivered by spontaneous vaginal delivery and this represents 6.25% (9/144) of those who were delivered per vaginal compared to one case (10%) who had caesarean section representing 7.1% (1/14) of those delivered by this method. One hundred and forty eight (93.7%) of the babies tested negative to HIV and were discharged from ART clinic after the second PCR at one year of age, while the remaining 10 (6.3%) tested positive and were enrolled for antiretroviral therapy. One (10%) of the ten babies with positive PCR result was delivered in private hospital, two (20%) at home, and the remaining 7 (70%) in government hospitals. Majority (60%) of the 10 positive infants did not receive Nevirapine in the first 6 weeks of life while the remaining four (40%) did. Most (90%) of the positive infants were breastfed exclusively while one (10%) had breast milk substitute and none had mixed feeding. Four of them were male while six were females.

Discussion

The prevalence of DNA PCR reactivity among HIV-exposed infants in EksUTH, Ado-Ekiti, Nigeria was 6.3% (Table I). This is comparable to the finding of 6.5% in a similar study in Zambia^[13] and 5.8% in Cape town, South Africa.^[14] It is however higher than 1.8% prevalence reported by Onakpa and Tahir^[10] in Sokoto, Nigeria. Reason for this difference could partly be due to the difference in duration of the study. The study from Sokoto covered a 24 month period while the present study covered a 5 year period. Also, the present study included exposed babies referred from other health facilities, while that of Sokoto was restricted to infants of HIV-positive mothers who had ANC and participated in PMTCT program in the facility. Also, the proportion of HIV-positive mothers who never received HAART during pregnancy (8.9%) in the present study is higher than 7% reported by Onankpa and Tahir.^[10]

HIV positivity rate among infants of HIV-positive mothers was higher (28.6%) in babies whose mothers did not receive HAART during pregnancy compared to those whose mothers commenced during pregnancy (5.4%) and it was lowest (3.4%) in those whose mothers commenced HAART before pregnancy and the difference was statistically significant ($p = 0.01$). This finding is consistent with findings from previous studies.^[10,15] Positive HIV reactivity rate in exposed infants seen in EkSUTH is high and is a call for intensified effort to reaching out to women of child-bearing age and ensuring all pregnant women are screened for HIV early and commenced on HAART if need be. Also, all babies should be routinely screened for HIV at birth as a way of identifying mothers who may have been missed during pregnancy and also for early enrolment of exposed babies for EID.

Majority (89.9%) of the infants in the present study were exclusively breastfed, and this is consistent with findings in the Northern part of Nigeria^[10] and Zambia^[15] where proportion of HIV exposed-infants who were exclusively breastfed was reported as 85.3% and 84.0% respectively. Although nine of the infants who tested positive to HIV were exclusively breastfed, this study showed that breastfeeding did not increase the likelihood of an infant testing positive to HIV. It is however noteworthy that 1.9% of our studied exposed infants had mixed feeding and all of them tested negative to HIV. This is surprising as other researchers have highlighted the high risk of mother to child transmission in the mixed feeding method.^[6,10,16] It could be explained by the fact that we had a mixed population of babies delivered within and outside EkSUTH whose mothers probably didn't receive proper counseling on feeding options prior to their delivery as some were actually referred to the centre after the delivery even though continuous counseling on feeding methods were integral parts of the care package given to the mothers during the treatment. There is therefore the need to extend teaching on EID and feeding of HIV-exposed babies beyond the walls of teaching hospitals to other places where deliveries take place; since 60% of all deliveries takes place where there are no skilled

care.^[17,18] It must however, be stated clearly that only exclusive breastfeeding and/or feeding with breast milk substitute alone has been shown to be safer than mixed feeding as a feeding option for infants of HIV positive mothers.^[9] Early mixed feeding has been associated with four-fold risk of HIV transmission at six months of age for HIV-exposed babies who previously tested negative at six weeks of age.^[6,10,16]

The proportion of discordant couples in the present study was 39.9% while the HIV status of majority (57.6%) of the fathers was unknown. This may be a pointer to lack of family support for HIV-positive mothers and their exposed babies, which may encourage mixed feeding and non-compliance with treatment in a bid to hide their HIV status from their husbands and relatives, thereby increasing the risk of infection in the exposed babies.

There seems to be no comparative advantage regarding whether the exposed infants were delivered per vaginal or through Caesarean section. This is reassuring for mothers and families with HIV positivity who might have been made to believe that operative delivery better protects against the risk of MTCT of HIV.^[19-21] Though our findings report the results from one center and further expansion may be needed to ascertain the generalizability of these observations, it is nevertheless reassuring for the people living in third world countries for whom such delivery method may be too costly to bear in terms of the financial implications and the attendant huge morbidity and even mortality that could follow the method of delivery. Therefore, our findings underscore the fact that, given appropriate timely treatments, mothers with HIV infection need not be subjected to needless Caesarean sections, if not clinically indicated. Also, universal precaution and safety should be maintained during any invasive surgical procedure.

Administration of Nevirapine for the first 6 weeks of life to HIV-exposed infants significantly contributed to prevention of infection in the present study: few (2.7%) of those who received Nevirapine in the first 6 weeks of life had positive PCR results compared to 54.5% of those who did not and the

difference was statistically significant ($p = 0.001$). There is need to encourage the government and global health donors funding organizations and partners to ensure availability of this drug for all exposed babies so as to ensure the effectiveness of the PMTCT program. Prior studies have reported the importance of global health donor funding in the reduction of HIV prevalence in developing countries.^[22,23] Moreover, in view of global economic recession with greater impact on developing countries, where more people are living with HIV,^[1,9] global health donors should sustain their efforts in assisting developing countries combat the HIV pandemic.

Conclusions and Global Health Implications

Positive reaction to PCR in HIV-exposed infants seen at EkSUTH is relatively high; however commencement of HAART in HIV-positive mothers before pregnancy and administration of Nevirapine to exposed babies for the first 6 weeks of life significantly reduced transmission of HIV from mothers to children. There is need for more sustained efforts at optimizing early infant diagnosis at ART centers in low and middle-income countries through increased supports from governments and other stakeholders.

Conflict of Interest: *The authors declare that they have no conflict of interest relevant to this study.*

Acknowledgement: *The authors appreciate the Institute of Human Virology of Nigeria for sponsoring PCR analysis and the clinical and laboratory staffs of EkSUTH for their contribution. We also appreciate the staff of the clinical units for keeping the records that were used in the analyses presented in this paper.*

Key Messages

- The effectiveness of PMTCT program can be greatly enhanced by extending early infant diagnosis and treatment to all babies delivered in health facilities outside teaching hospitals.
- There is an ongoing need for continued and sustained funding of HIV prevention and treatment programs in developing countries such as Nigeria.

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