Journal of Medicine and Medical Science Vol. 2(6) pp. 914-919, June 2011
Available online@ http://www.interesjournals.org/JMMS

Full Length Research Paper

Sero-reversion time of HIV exposed un-infected Nigeria Children

[1]*A. A Okechukwu and [2]O. I Okechukwu

*[1]Department of Paediatrics, University of Abuja Teaching Hospital, Gwagwalada, FCT, Abuja.
[2]Paediatric Outpatient Special Treatment Clinic, University of Abuja Teaching Hospital, Gwagwalada, FCT, Abuja.

Accepted 15 June, 2011

Maternal acquired HIV antibodies transferred during pregnancy from sero-positive mothers to their infants is expected to disappear before 18 months of postnatal life. To determine the time these maternal HIV antibodies transferred via the placental during pregnancy disappears from the blood of exposed uninfected Nigerian infants. A two year prospective study was carried out among HIV exposed uninfected children at the University of Abuja Teaching Hospital, Gwagwalada, Nigeria from November 2008 to October 2010 for the above objective. Of a total of 112 HIV exposed uninfected children studied, 57.1% were males and 42.9% female, m:f of 1.3:1. Greater than 28% of exposed uninfected infants sero-reverted before 6 months of age, 89 (79.5%) by 9 months, 110 (98.2%) by the 12th month, and 100.0% by 15 months. More males appeared to have sero-reverted than their female counterpart at 9 months of age, x^2=8.21, p=0.004. No association was seen between the other study variables and time of sero-reversion, *p* values > 0.05. Most HIV exposed uninfected Nigerian infants sero-reverted before 9 months of age. The study therefore advocates monthly serology test for exposed infants from 3 months to identifying early sero-reverters for possible discharge from the paediatric special treatment clinic in centres with no facility for DNA PCR test.

Keywords: HIV exposed, un-infected, sero-reversion, maternal antibody.

INTRODUCTION

Maternal HIV antibodies are passively transferred during pregnancy via placenta from sero-positive mothers to their babies (Chantry et al., 1995). In uninfected infants, antibodies disappear overtime and the child is said to have reverted to HIV sero-negative status (Lapointe et al., 1993). The time of disappearance of these maternal acquired antibodies also describe as sero-reversion time varies with individual and communities and can extend up to 18 months or more of postnatal life in some cases (Chantry et al., 1995; CDC, 1987: European Collaborative Study, 1991).

Serology testing for HIV infection in children born to infected mothers is constrained by the persistent of maternal antibodies which result in uninfected infants testing positive for HIV infection (Moodley et al.,1995; Simpson and Andiman, 1994). Rapid tests routinely used to determine the presence of these antibodies has been noted not to perform uniformly during infancy (Sherman et al 2008: Claassen et al., 2006). However, Determine was the only rapid test found to maintain sensitivity of 99.7% throughout infancy, exceeded that of the enzyme linked immuno-sorbent assay (ELISA) from 7 months of age (Sherman et al., 2008). Rapid test cannot distinguish between maternally acquired antibodies and the endogenous HIV antibodies produced by the infected infants, hence it is not recommended for diagnosis of HIV in children in the first 18 months of postnatal life. (Moodley et al.,1995; Rakusan et al., 1991; Simpson and Andiman, 1994). In 1987, the Centre for Disease Control and Prevention (CDC) published guidelines for diagnosis of HIV infection in children (CDC, 1987). The presence of HIV antibodies beyond 15 months in HIV exposed was

*Corresponding author E-mail: nebokest@yahoo.com

accepted as an indication of HIV infection using ELISA or Western blot test. The guideline was later revised in 1994 and extended the cut off age to 18 months using serology method. According to CDC, although HIV antibody usually became undetectable by 9 months of age, it can occasionally be detected up to 18 months of age in 1- 2% of un-infected infants.

This policy has been called to question by the observation that in communities with high prevalence of endemic HIV infection, maternal acquired antibodies may persist in HIV exposed negative children even beyond the recommend out off age for serology testing (Gulia et al., 2007; Ewang, 2007). When HIV prevalence is high and endemic in a community, a state of equilibrium is reached whereby maternally transferred HIV immunoglobulin G antibodies may persist for a longer time in the blood of HIV exposed uninfected infants (Levin et al., 2001). In support of the above statement was increase in sero-reversion time from 7 months (Andiman et al., 1990) to 11 months in the same centre after four years of initial assessment (Sampson and Andiman, 1994). At the four years interval, the HIV infection have reached the epidemic level in that community. This confirms the fact that the mean sero-reversion time can increase overtime (Gulia et al., 2007). Other factors noted to influence sero-reversion time include: birth weight (Gulia et al., 2007), CD4 cell count (Alcântara et al., 2009) and intrauterine antiretroviral drug exposure (Mary et al., 2005). Exposed uninfected infants born to AIDS mothers with lower $CD4^+$ T-cell counts has also been observed to sero-revert earlier than infants born to asymptomatic positive mothers. Reason suggested being possibility of maternal immunological status impacting on the time to seroreversion (Alcântara et al., 2009), as ongoing antigenic stimulation has being shown to maintain HIV-1-specific humoral responses. Early antiretroviral therapy associated with durable virologic suppression in acute HIV-1 infection has been observed to abrogate the formation or detection of HIV-1-specific antibodies (Mary et al., 2005) that will in turn influence the time of sero-reversion.

Although HIV has established itself in Nigeria with high prevalence ranging from 5.8% in 2001 to 4.4% in 2005, with a slight increase to 4.6% in 2008 (Federal Ministry of Health, 2008), there is currently no information on sero-reversion time of HIV exposed uninfected Nigerian children. It is on this background that the study was carried out to document the sero-reversion time of this group of children in the country. It is also aimed at determining any factor(s) affecting the time of disappearance of these maternal transferred antibodies in the environment. The result of the study we believe will not only provide baseline information on this group of infants since no such study has been carried out in the environment, but will also form basis for future comparison.

SUBJECTS AND METHODS

We carried out a 2 years prospective analysis of all deoxy-ribonucleic acid polymerase chain reaction (DNA PCR) negative, HIV exposed uninfected babies at the Paediatric Special Treatment Clinic (PSTC) of the University of Abuja Teaching Hospital (UATH), Gwagwalada to determine when they sero-revert to negative status. UATH is a 350 bed referred hospital that serves the people in Federal Capital Territory (FCT), Abuja and four adjoining states of Nasarrawa, Kogi, Niger, and part of Kaduna state. PSTC is an out-patient delivery unit providing clinical serves to HIV infected/exposed children at the health institution. Exposed children are followed up at this special clinic for their neonatal post exposure prophylaxis with anti-retroviral drugs according to National guide line on Paediartric HIV/AIDS treatment and care (Federal Ministry of Health 2008), co-trimoxazol prophylaxis, continuous counselling/support on infant feeding, and growth monitoring until they are confirmed uninfected.

The subjects are HIV exposed, DNA PCR negative babies. DNA PCR test amplifies and detects the HIV pro-viral DNA sequences within the mononuclear cells in the blood, it is a gold standard test for diagnosis of HIV infection in infants in developed countries (Tindyebwa et al., 2004; Federal Ministry of Health, 2008). The test is 100 percent sensitive by 4 to 6 weeks of postnatal life (Tindyebwa et al., 2004; Federal Ministry of Health 2008; Benjamin et al., 2001). Monthly serology was carried out for all negative recruited infants from the age of 3 months to 12 months, and thereafter on a 3 monthly bases until their 18 months birth day. Sera obtained from the patients were screened for the presence of HIV 1 or 2 antibodies using serial immunochromatographic qualitative tests [National Serial Algorithm 11] recommended by (Federal Ministry of Health 2008: World Health Organisation 2006) with commercially available recombinant antigen based rapid tests (*DETERMINE by Abbot Laboratories Japan, STATPAK by Chembio diagnostic system INC New York, and UNIGOLD by Trinity Biotech Plc Bray, Ireland*) with sensitivity and specificity of 100%. Serial testing implies performing a second confirmatory test after an initial positive test. The test kits use the same principle of patient's blood migrating through the conjugate pad to mix with the colloid-antigen conjugate. The presence of antibodies to HIV 1 and 2 in the patient's blood will bind to the antigen to the form a colour line in patient's window. The test procedure involve the use DETERMINE as the first test kit, and when positive is further subjected to second testing with a second test kit, (UNIGOLD), which when positive implies that the patient is HIV positive. But when the second test result is negative with UNIGOLD test kit, the sample will be further tested with the third test kit (STAT PAK), and when positive confirms positive nature of the sample. When the initial first test kit

Table 1: Characteristics of the study population

Characteristic n = 112 (%)	Study Population	P valve
Sex		
Male	64 (57.1)	>0.05
Female	48 (42.8)	
Gestational age		
< 37 wks	27 (24.1)	<0.05
37 – 42 wks	85 (75.9)	
Birth Weight		
<2.5	25 (22.3)	<0.05
2.5 – 3.9	87(74.1)	
Mode of Delivery		
Vaginal	97(81.6)	<0.001
Caesarean Section	15(13.4)	
Mode of Feeding		
Breast feeding	19(5.4)	<0.001
Artificially feed	93(83.0)	
Mothers ARVT in Pregnancy		
Yes	101 (90.2)	<0.001
No	11 (9.8)	
NPEP		
Yes	109 (97.3)	<0.001
No	3 (2.8)	

ARVT antiretroviral therapy
NPEP: Neonatal Post Exposure Prophylaxis

Table 2: Proportion of Children Who Sero-reverted at Various Months

Time of Rapid Test (months)	Proportion that Sero-reverted (%)
3	1(0.9)
4	5(4.5)
5	15(13.4)
6	32(29.5)
7	35(31.3)
8	73(65.2)
9	89(79.5)
10	96(85.7)
11	99(88.4)
12	110(98.2)
15	112(100.0)

(DETERMINE) is negative, the sample is said to be negative and will not be subjected to further testing (Federal Ministry of Health 2008: World Health Organisation 2006).

Information collected includes: sex, gestational age, age at sero-reversion, birth weight, history of maternal anti retroviral therapy during pregnancy, mode of delivery, history of neonatal post exposure prophylaxis, and method of infant feeding. The anti retroviral drugs used by the mothers who needed treatment for their own HIV disease during pregnancy were combinations of zidovudine, lamivudine, nevirapine or efavirenz (Federal Ministry of health, 2007). Efavirenz was used in place of nevirapine for those with tuberculosis (TB)/ HIV co-infection. Tenifovir, lamivudine or emtricitabine, neviprapine or efavirenz were used for those mothers with haemoglobin of <8gm/dl, or those with HIV/hepatitis B co-infection. For HIV pregnant mothers who do not need treatment for their HIV infection, zidovudine alone was started at 28 weeks of pregnancy, or zidovudine and lamivudine at 34-36 weeks. All groups of mothers received intrapartum nevirapine, zidovudine, lamivudine, as well as zidovudine and lamivudine for 7 days after delivery (Federal Ministry of health, 2007). The anti retroviral drugs used for neonatal post exposure prophylaxis were zidovudine for 6weeks and start dose of nevirapine at birth (Federal Ministry of health, 2008).

Ethical approval was obtained from the ethic committed of the hospital before the study. Data analysis was computed using Epi info version 3.2.2 of April 14, 2004 which provided frequency distribution, test of significance.

RESULT

The characteristic of exposed uninfected recruited infants was shown in table 1. Of a total of 112 recruited babies, 64 (57.1%) were males and 48 (42.8%) females given a male: female ratio of 1.3:1. 24.1% of the these babies were preterm deliveries, 22.3% were less than 2.5kg, and greater than 80% were artificially fed and delivered vaginally. More than 95% received neonatal post exposure prophylaxis of antiretroviral drugs soon after delivery, while > 90% of their mothers' received antiretroviral drugs during pregnancy.

Table 2 shows the proportion of children who sero-

Table 3: Sero-reversion at 9, 12 and 15 months and various variables studied.

Variables	RST by 9mths (n=89)		RST by 12mths (n=110)		RST by 15mths (n=112)	
	Sero reverted	Not Sero Reverted	Sero reverted	Not sero reverted	Sero reverted	Not sero reverted
Gender						
Male	51	13	63	1	64	0
Female	38	10	47	1	48	0
Gestational age (<37weeks)						
Male	6	10	15	1	16	0
Female	4	6	9	1	10	0
(>37weeks)						
Male	45	3	48	0	48	0
Female	34	4	38	0	38	0
Birth weight (<2.5kg)						
Male	10	11	19	2	21	0
Female	8	5	13	0	13	0
(<2.5kg)						
Male	41	2	43	0	43	0
Female	30	5	35	0	35	0
Mode of feeding (Breast feeding)						
Male	2	7	8	1	9	0
Female	4	6	9	1	10	0
(Artificial feeding)						
Male	49	6	55	0	55	0
Female	34	4	38	0	38	0
Mode of Delivery (Vaginal)						
Male	42	9	51	0	51	0
Female	31	7	36	2	38	0
(C/S)						
Male	9	4	13	0	13	0
Female	7	3	10	0	10	0
Mother on ARDs (Yes)						
Male	51	7	58	0	58	0
Female	38	3	41	0	41	0
(No)						
Male	0	6	6	0	6	0
Female	0	7	5	2	7	0
NPEP (Yes)						
Male	51	10	61	0	61	0
Female	38	10	48	0	48	0
(No)						
Male	0	3	1	2	3	0
Female	0	0	0	0	0	0

ARDsVT – Antiretroviral
RST : Rapid Serology Test.
NPEP: Neonatal Post Exposure Prophylaxis

reverted by age in months and sex. More than 75% of HIV exposed uninfected Nigerian infants sero-reverted before their 9th month's birth day. By the age of 6 months, 32 (29.5%) of babies had sero-revered to negative status, at 9 months 89 (79.5%) has sero-reverted, 110 (98.2%) by 12 months, and 112 (100%) by 15 months..

Table 3 showed babies that sero-reverted at 9, 12, 15, against the various study variables by sex. By the age

of 9 months, more preterm babies, those less than 2.5kg, those delivered by caesarian section, artificially fed babies, and babies whose mothers did not receive any anti-retroviral medication during pregnancy has not sero-reverted when compared to their counterpart. By the age of 12 months majority of the babies has sero-reverted against all the variables studied, and by 15 months all the study infants have sero-reverted. Sex was the only study variable found to have significant association with time of sero-reversion, more males appeared to have sero-reverted more than their female counterpart at 9 months, x^2 =8.21, p value 0.004. No other variables was seen to have such association with the time of sero-reversion, p values >0.05.

DISCUSSION

From the result of the study, greater than 28% of uninfected infants sero-reverted between 3 to 6 months, and 80% before the age of 9 month using rapid test. This was similar to the findings from Uganda study were rapid tests was found to rule out HIV infection in more than 30% of infants at 3 to 6 months and 66% at 6 to 9 months of age (Homsy et al., 2007). It was also similar to the findings by (Sohn et al., 2009) who also noted >90% of uninfected infants sero-reverting by 12 months of age using enzyme immunoassay (EIA). The mean and/or median age at the time of seroreversion ranges between 9 months to 16 months of age in studies from both Western and resource-limited countries (Chantry et al., 1995; Andiman et al.,1990; European Collaborative Study 1991; Sherman et al., 2000: Jones et al., 2005; Palasanthiran et al., 1994). These data indicate that maternal antibody levels of HIV antibody remain detectable through the first 6 months of life but decay significantly by 9-12 months of age, and most cases undetectable by one year of life. While the majority of uninfected non-breastfed children will have cleared maternal antibody by age 12 months, a small percentage of children do not serorevert until age 18 months (Chantry et al., 1995; Andiman et al., 1990) and in rare instances even beyond 18 months (European Collaborative Study 1991). No such delayed sero-reversion beyond 15 months was observed in the present study. Several other workers have also reported different period of sero-reversion with different serology method (Lapointi et al., 1993; Louisirirotchanakul et al., 2002). It does appear that time of sero-reversion is predetermined by the type of serology method. Using the ELIZA, (Chantry et al., 1995) reported mean sero-reversion time at 11.6 months, however when Western blot test was used in the same sample, sero-reversion time was noticed at 15.8 months. Because of variation in time of sero-reversion using different serology method, the authors supports the earlier suggestion by (Sohn et al., 2009), who advocated the need for reassessing the performance of standard EIAs test regarding infant seroreversion to reflected potential cross-regional differences.

The present study showed that up to 18.8% of uninfected infants sero-reverted before their 6th month birth day. Mary et al (2005) while looking at incomplete HIV Type 1 antibody evolution and seroreversion pointed out that intrauterine antiretroviral exposure influences time of seroreversion, possibility of effect of antiretroviral on maternal immunological status via its viral suppressive activities, as ongoing antigenic stimulation has being shown to maintain HIV-1-specific humoral responses. Even though no such relationship was recorded in the present study, undocumented situations (eg low maternal HIV antibody titer) may be responsible for early sero-reverting in some babies. Several literature evidence (Chantry et al., 1995; Andiman et al., 1990; Simpson et al., 1994; Ewang, 2007), have also reported sero-reversion occurring latter during epidemic phase of HIV infection. To buttress the above statement is the variation in age of disappearance of maternal transferred antibodies from viral infection like measles (Maldonado et al., 1995; Szenborn et al., 2003). Early disappearance of maternal antibodies is said to occur in infants whose mothers received measle vaccine, than those who had natural infection (Maldonado et al., 1995; Szenborn et al., 2003). Measle vaccines is said to induce a lower antibody titer level than the natural infection, and hence persist for a shorter period (Szenborn et al., 2003). The duration at which measle antibodies persist is proportional to the antibody titer passed to the infants from their mothers (Szenborn et al., 2003). HIV and measles infections are both viral in origin, and both induce antibody that is transferred to their unborn children transplacementally (Szenborn et al., 2003; Kolleman et al., 1991). Even though HIV antibody titer was not measured at birth and thereafter in the present study, going by the finding in measles antibodies whose persistence is proportional to the antibody titer passed to infants, early disappearance of maternal HIV antibody in over 75% of un-infected infants by the age of 9 months in the present study might be as a result of low antibody titer passed on to these infants from their mothers who may have not been seriously handicapped by HIV infection.

Sex is the only study variable found to have association with time of sero-reversion at 9 months of age. More males appeared to have sero-reverted more than their female counterpart at 9 months of age. Though no such association has been documented in any study, however, many others workers have noticed significant association between sero-reversion time and birth weight (Gulia et al., 2007), CD4 cell count (Alcântara et al, 2009) and intrauterine antiretroviral drug exposure (Mary et al., 2005), and attributed their findings to lower immunologic response from low antigenic exposure in babies with higher birth weight, and possibility of lower maternal immunological status impacting on the time to sero-

reversion with lower CD4 cell count, and intrauterine antiretroviral drug exposure.

CONCLUSION

Most HIV exposed uninfected Nigerian infants sero-reverted before 9 months of age. The study therefore advocates monthly serology test for HIV exposed infants from 3 months to identifying early sero-reverters for possible discharge from the clinic in centres with no facility for DNA PCR test.

REFERENCES

Alcântara KC, Pereira GA, Albuquerque M, Stefani MA (2009). Seroreversion in children born to HIV-positive and AIDS mothers from Central West Brazil Summary. Transactions of the Royal Society of Tropical Medicine and Hygiene; 103 (6) 620-626.

Andiman WA, Simpson BJ, Olson B (1990). Rate of transmission of human immunodeficiency virus type I nfection from mother to child and short term outcome of neonatal infection. Results of a prospective cohort study. M J Dis child. 144(7) : 758 – 66.

Benjamin DK, Miller WC, Susan A. Fiscus SA, Morse M, Valentine M et al (2001). Rational Testing of the HIV-Exposed Infant. Pediatrics; 108 (1) e3 (doi: 10.1542/peds.108.1.e3).

Center for Disease Control Prevention (1987). Classification system for human immunodeficiency virus (HIV) infection in children under 13 years of age. MMWR Morb Mortal Ekly Rep. 1087; 36; 225 – 230, 235-236.

Chantry CJ, Cooper ER, Pelton SI Zorilla C, Hillyer GV, Diaz C (1995). Sero-reversion in human immunodeficiency virus exposed but uninfected infants. PIDJ.;14: 382-387.

Claassen M, Van Zyl GU, Korsman SN, Smit L, Cotton MF, Preiser W (2006). Pitfalls with rapid HIV antibody testing in HIV-infected children in the Western Cape, South Africa. J. Clin. Virol., 37(1):68–71.

Eberle J, Notheis G, Blattmann C, Jung J, Buchholz, B, Korn K et al (2010). Seroreversion in vertically HIV-1-infected children treated early and efficiently: rule or exception? AIDS: 24(17):2760-2761.

European Collaborative Study (1991). Children born to women with HIV-1 infection: natural history and risk of transmission. Lancet; 337(8736):253-60.

Ewang T (2007). Is serology testing for HIV at 18 months of age in children born to HIV infected mothers still reliable? AIDS map News No. 16.

Federal Ministry of Health (2007). National Guide line on Prevention of Mother-to Child Transmission of HIV (PMTCT),

Federal Ministry of Heath Nigeria (2008). National guideline for Paediatric HIV and AIDS.

Gulia J, Newton K, Quig L, Taha TA (2007). HIV seroreversion time in HIV-1-uninfected children born to HIV-1-infected mothers in Malawi. J Acquir Immune Defic Syndr;46(3):332–337.

Homsy J, Downing R, Finkbeiner T (2007). The use of rapid testing prior to DNA PCR for early screening of HIV infection in infants in Uganda. Paper presented at: CROI 2007; February 25-27, Los Angeles, CA.

Jones SA, Sherman GG, Coovadia AH (2005). Can clinical algorithms deliver an accurate diagnosis of HIV infection in infancy? Bull World Health Organ., 83(7):559-60.

Lapointe N, Fauvel M, Deziel E, Samson J, Boucher M Hankin C (1993). Seroreversion of non-infected children born to HIV infected mother. Int conf. AIDS June 6-11, 9:277 (abstract No. PO – BOI0855).

Levin BR, Bull JJ, Stewart FM (2001). Epidermiology, evolution, and future of the HIV/AIDS Pandemic. Emerg Dis.; 7 (3 suppl): 505-511.

Louisirirotchanakul S, Kanoksinsombat C, Likanonsakul S, Sunthornkachit R, Supanit I, Wasi C (2002). Patterns of anti-HIV IgG3, IgA and p24Ag in perinatally HIV-1 infected infants. Asian Pac J Allergy Immunol 2002;20:99-104.

Maldonado YA, Lawrence EC, De Hovtz (1995). Early loss of passive measle antibody in infants of mothers with vaccine induced immunity. Pediatrics 96: 477-450.

Mary NS, JohnstonEric S, Rosenberg Y (2005). Incomplete HIV Type 1 Antibody Evolution and Seroreversion in Acutely Infected Individuals Treated with Early Antiretroviral Therapy. Clinical Infectious Diseases :40 (6): 868-873.

Palasanthiran P, Robertson P, Ziegler JB, Graham GG (1994). Decay of transplacental human immunodeficiency virus type 1 antibodies in neonates and infants. J. Infect. Dis., 170(6):1593-6.

Pierce VM, Neide B, Richard L (2011). Hodinka LR. Evaluation of the Gen-Probe Aptima HIV-1 RNA Qualitative Assay as an Alternative to Western Blot Analysis for Confirmation of HIV Infection. J. Clinical Microbiol., 49 (4): 1642-1645.

Sherman GG, Stevens WS, Stevens G, Galpin JS (2000). Diagnosis of human immunodeficiency virus infection in perinatally exposed orphaned infants in a resource-poor setting. Pediatr Infect Dis J., 19(10):1014-5.

GG, Driver GA, Coovadiac AH (2008). Evaluation of seven rapid HIV tests to detect HIV-exposure and seroreversion during infancy. J. Clin. Virol., 43 (3): 313-316.

Simpson BJ, Andiman WA (1994). Difficulties in assigning human immune-deficiency virous-1 infection and seroreversion status in a cohort of HIV-exposed in children using serologic criteria established by the centers for Diseae control and prevention. Pediatric. 93: 840-842.

Sohn HA, Thanh TC, Thinh LQ, Khanh TH, Thu HK, Giang, LT et al (2009). Failure of Human Immunodeficiency Virus Enzyme Immunoassay to Rule Out Infection Among Polymerase Chain Reaction-Negative Vietnamese Infants at 12 Months of Age. Pediatric Infectious Disease J., : 28 (4): 273-276..

Szenborn L, Tischer A, Pejez J (2003). Passive acquired immunity against measle in infants born to national infected and vaccinated mothers. Med. Sci. Monit.; 9: CR 541-CR546

Tindyebwa D, Kayita J, Musoke P, Eley B, Nduati R et al (2004). Handbook of Paediatric AIDS in Africa by the African Network for the care of children Affected by AID. pg 79-82 . www.rcghc.org.

World Health Organisation (2006). Recommendations on the Diagnosis of HIV Infection in Infants and Children. Draft for Public View (Ver 6), July 2006, pp7-24.