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Original Investigation / Özgün Araştırma

90–90–90 targets: Reaching the first 90 diagnosing exposed babies using the virologic HIV DNA nucleic acid–based technique

90–90–90 hedefleri: Virolojik HIV DNA nükleik asit bazlı teknik kullanarak enfekte olan bebeklerin yüzde 90 teşhis edilmesi

Saheed Opeyemi Usman, Ganiyu Babatunde Agboola, Florence Chinwe Umeozulu
Department of Clinical Laboratory, Equitable Health Access Initiative, Lagos, Nigeria

ABSTRACT

Objective: The HIV pandemic has continued to be a huge challenge in Nigeria, with the problem of stigmatization reducing the chances of early determination of HIV status in pregnant women, which may increase the chances of transmission to the child from the mother. Our study was designed to determine the trend as well as diagnosis of HIV infection in exposed infants. It will also determine among infants the factors associated with the transmission of the infection from their mothers.

Methods: This was a study of HIV-exposed infants conducted between January 2013 and December 2015. The study population was HIV-exposed infants. Dried blood spots (DBS) were analyzed using the polymerase chain reaction technique.

Results: Only 18.3%, 20.1%, and 14.2% of the babies had their DBS samples taken at six weeks of age in 2013, 2014, and 2015, respectively. The percentage of positives across the three years was 3.6%, 3.2%, and 3.1%, as the majority of the babies took single-dose nevirapine and had exclusive breastfeeding, but only 1.5% and 1.3% of the babies within 18-month PMTCT retested for 2013 and 2014 were confirmed positive after cessation of all exposures.

Conclusion: ART administration to both HIV-infected mothers and their babies has demonstrated an effective mechanism of the PMTCT program, as this is evident in the low positivity outcome. However, the feat of mother-to-baby HIV transmission elimination achieved by Cuba, Armenia, Belarus, and Thailand is achievable in Nigeria through provision of universal access to health care.

Keywords: PMTCT, HAART, infant, dried blood spot, polymerase chain reaction

ÖZ

Amaç: HIV salgını, hamilelerde erken tespit şansını azaltan ve anneden çocuğa geçme olasılığını artırabilecek damgalama ile birlikte, Nijerya'da büyük bir problem olmaya devam etmektedir. Çalışmamız etkilenen bebeklerde HIV enfeksiyonunun tanısının yanı sıra eğilimi belirlemek amacıyla dizayn edilmiştir. Ayrıca, çocuklarda annelerden enfeksiyon geçişi ile ilişkili faktörler de çalışmada tespit edilecektir.

Yöntemler: Bu çalışma Ocak 2013 ve Aralık 2015 tarihleri arasında HIV'den etkilenen çocuklarla yapıldı. Çalışma popülasyonunu HIV'e maruz kalan çocuklar oluşturdu. Kuru kan lekeleri (DBS) polimeraz zincir reaksiyonu tekniği kullanılarak analiz edildi.

Bulgular: Bebeklerin sadece %18,3, %20,1 ve %14,2'sinin ilk altı haftalarında kuru kan lekesi örnekleri sırasıyla 2013, 2014 ve 2015 yıllarında alındı. Üç yıldaki pozitiflik yüzdesi %3,6, %3,2 ve %3,1 olarak bulunan bebeklerin çoğunluğu tek doz nevirapin alıyordu ve sadece anne sütü ile besleniyordu. Ancak, 18 ayda PMTCT (prevention of mother-to-child transmission: anneden çocuğa HIV geçişinin önlenmesi) kapsamında 2013 ve 2014 yıllarında tekrar test edilen bebeklerin sadece %1,5 ve %1,3'ü tüm risk maruziyetlerin kesilmesi sonrasında pozitif olarak bulundu.

Sonuç: HIV-enfekte annelerde ve bebeklerinde ART (antiretroviral therapy) uygulaması PMTCT programının etkili bir mekanizmasını göstermiştir ve bu da düşük pozitiflik sonucunda belirgindir. Ancak, Küba, Ermenistan, Belarus ve Tayland tarafından gerçekleştirilen anneden bebeğe HIV geçişinin önlenmesi başarısı evrensel sağlık bakımına erişim şartıyla Nijerya'da mümkündür.

Anahtar kelimeler: PMTCT, HAART, bebek, kuru kan lekesi, polimeraz zincir reaksiyon

INTRODUCTION

Approximately 370,000 infants were infected with Human Immunodeficiency Virus (HIV) worldwide in 2009 via transmission to the child from mother, with an estimated two and half million children infected worldwide generally, majority of who live in sub-Saharan Africa (1, 2). Mothers can infect their children when still in the uterus, when they give birth or after birth during breastfeeding. Thus, interventions are directed towards these above-mentioned periods, especially with anti-retroviral therapy use. The transmission risk reduces to around 1-2% with combination of these strategies, while a neglect of the strategies put 30-45% the children at infection risk, with around 10-20% infected through breastfeeding (3, 4). Anti-retroviral therapy administered on pregnant women positive to HIV as well as

Corresponding Author/Sorumlu Yazar: Saheed Opeyemi Usman **E-mail/E-posta:** senatorhopsy@yahoo.com
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Tablo 1. Characteristics of infants and mothers

Characteristics	Jan-Dec 2013		Jan-Dec 2014		Jan-Dec 2015	
	Frequency	%	Frequency	%	Frequency	%
Sex						
Male	301	54.6%	191	48.0%	276	53.6%
Female	250	45.4%	207	52.0%	239	46.4%
Age (weeks)						
6 weeks	101	18.3%	80	20.1%	73	14.2%
>6-12 weeks	206	37.4%	117	29.4%	223	43.3%
>12-24 weeks	98	17.8%	78	19.6%	65	12.6%
>24-48 weeks	66	12.0%	63	15.8%	80	15.5%
>48-72 weeks	80	14.5%	60	15.1%	74	14.4%
Eid result						
Negative: Male	288	52.3%	184	46.2%	269	52.2%
Female	243	44.1%	201	50.5%	230	44.7%
Positive: Male	13	2.3%	7	1.8%	7	1.4%
Female	7	1.3%	6	1.5%	9	1.7%
Total positive	20	3.6%	13	3.2%	16	3.1%
Infant ARVs						
Single dose nevirapine	509	92.4%	369	92.7%	497	96.5%
No ARV taken	10	1.8%	8	2.0%	7	1.4%
Unspecified	32	5.8%	21	5.3%	11	2.1%
Infant ever breastfed						
Yes	530	96.2%	385	96.8%	501	97.3%
No	21	3.8%	13	3.2%	14	2.7%
Type of breastfeeding						
Exclusively breastmilk	495	89.8%	366	92.0%	459	89.1%
Replacement feeding	21	3.8%	15	3.8%	30	5.8%
Mixed feeding	29	5.3%	14	3.5%	18	3.5%
Unspecified	6	1.1%	3	0.7%	8	1.6%
Martenal ARVs						
HAART started before pregnancy	428	77.7%	317	79.6%	416	80.8%
HAART started during pregnancy	103	18.7%	61	15.3%	77	15.0%
No HAART taken	13	2.3%	11	2.8%	11	2.1%
Unspecified	7	1.3%	9	2.3%	11	2.1%
Place of delivery						
Primary	233	42.3%	152	38.2%	263	51.1%
Secondary	206	37.4%	148	37.2%	144	28.0%
Tertiary	112	20.3%	98	24.6%	108	20.9%
Rapid test results for babies >9 months						
Negative	68	12.3%	42	10.6%	69	13.4%
Positive	20	3.6%	18	4.5%	24	4.7%

ARVs: antiretrovirals; HAART: highly active antiretroviral therapy

Tablo 2. Age distribution and EID outcome

	Jan-Dec 2013			Jan-Dec 2014			Jan-Dec 2015		
	HIV−VE	HIV+VE		HIV−VE	HIV+VE		HIV−VE	HIV+VE	
Age (weeks)	Frequency (%)	Frequency (%)	Total	Frequency (%)	Frequency (%)	Total	Frequency (%)	Frequency (%)	Total
6 weeks	100 (18.2%)	1 (0.2%)	101	79 (19.8%)	1 (0.3%)	80	72 (14.0%)	1 (0.2%)	73
>6-12 weeks	205 (37.2%)	1 (0.2%)	206	117 (29.4%)	0 (0%)	117	221 (42.9%)	2 (0.4%)	223
>12-24 weeks	93 (16.9%)	5 (0.9%)	98	74 (18.6%)	4 (1.0%)	78	61 (11.8%)	4 (0.8%)	65
>24-48 weeks	59 (10.7%)	7 (1.2%)	66	58 (14.6%)	5 (1.2%)	63	75 (14.6%)	5 (0.9%)	80
>48-72 weeks	74 (13.4%)	6 (1.1%)	80	57 (14.3%)	3 (0.8%)	60	70 (13.6%)	4 (0.8%)	74
TOTAL	531 (96.4%)	20 (3.6%)	551 (100%)	385 (96.7%)	13 (3.3%)	398(100%)	499 (96.9%)	16 (3.1%)	515 (100%)
	χ^2=21.050, p=0.001			χ^2=10.775, p=0.029			χ^2=10.279, p=0.036		

The relationship is statistically significant at p<0.05 and very significant at p<0.01

their babies reduce infection risk from mother to child (5-7). In poor countries, about half of the infants infected with HIV but have no treatment die before their second birthday (8). Certain research work on HIV/AIDS and risk assessment in Nigeria reported 56.3% and 66.9% of informal and formal sector workers respectively are aware of the transmission of HIV to children from the mother (9, 10).

Maternal antibodies cross into the blood of infants, born by women infected by HIV, from the placenta. These antibodies often remain there until around one and half years, thus, making virological investigations more suitable for the infants during this period (11). Dried blood spot (DBS) is the sampling technique for infants exposed to HIV. Infants can be tested from six weeks of age and sample collection is from finger, toe or heel depending on the age and weight of the baby (12). This research was designed to determine the trend as well as diagnosis of HIV infection in exposed infants. It will also determine among infants the factors associated with the transmission of the infection from their mothers. A research work published in 2014 on the impact of HIV Prevention of Mother-to-Child Transmission of HIV (PMTCT) reported 7.0% of the children to be positive, with prevalence highest in the 6-18 months age group (16.1%) (13). An overall prevalence of 16.98% of postnatal HIV was observed in a study on PMTCT published in 2010 (14). In Tanzania, an overall MTCT prevalence rate of 6.3% was reported; 86.5% of these infants were exclusively breastfed at the time of first DBS sampling using the PCR technique (15). Another research in eastern Cameroon, published in 2013, reported that 50% of the infants were exclusively breastfed and based on the first PCR tests data, an overall prevalence of 11.6% was reported (16). In 2010, a study carried out in Malawi showed that 13.8% of children born by HIV-positive mothers turned out to be HIV-positive (17). In China, the mean rate of infants exposed to HIV was reported as 4.4% (18).

METHODS

Our study was conducted retrospectively on infants exposed to HIV enrolled secondary and tertiary level hospitals across Ondo State between January 2013 and December 2015. Study population was HIV-exposed infants, within the three year period (January 2013 to December 2015). Dried Blood Spot (DBS) specimen was collected from each infant and analysed with an automated real-time amplification and detection of Deoxyribonucleic Acid (DNA) using a qualitative DNA polymerase chain reaction (PCR), Cobas Taqman 48 analyser by (Roche Molecular Diagnostics , Basel, Switzerland). Statistical analysis of data was done using Statistical Package for the Social Sciences (SPSS) version 21. All variables had their frequency counts generated. Chi-square test was used for the statistical test for significance. The cities & country of the company are Akure & Lagos, Nigeria. Ethical approval was obtained from the Ondo State Ministry of Health Research Ethics Committee, Akure, Nigeria. Informed consent was obtained from all participants.

RESULTS

A total of 551, 398 and 515 HIV-exposed infants underwent the test each of the three years from January 2013 and December 2015. The research outcomes showed that majority of the children across the three years were breastfed exclusively and took single dose nevirapine while most of the mothers took antiretroviral therapy prior to pregnancy. Less than 5% of the infants tested positive for the early infant diagnosis test.

The full results are captured in tables.

DISCUSSION

The outcome of this study reveals a prevalence rate of 3.6%, 3.2% and 3.1% respectively as in Table 1 in 2013, 2014 and 2015 respectively. The prevalence across the three years is lower than those reported in various other studies. In Abuja Nigeria, a prevalence of 9.1% was reported while authors of a 2014 research work revealed 7.0% prevalence rate (13, 19). Also, an overall prevalence of 16.98% was reported in another 2010 publication (14). Prevalence rate of 6.3%, 11.6%, 13.8% and 4.4% were reported in Tanzania, Eastern Cameroon, Malawi and China respectively (15-18). This prevalence outcome is a tremendous improvement over all of the previous studies. The improvement might be attributed to enhanced spread of programmes targeting the prevention of HIV infection to children through the mothers especially with

utilization of updated guidelines where most positive mothers are on antiretroviral (ARV) therapy either before pregnancy or commenced during pregnancy, with a minimum of 94.9% of the mothers on ARV therapy across the three years under review, showing strict adherence to the PMTCT protocol, which has its main role in reducing HIV transmission. This outcome suggests therefore that the commencement of ARV prior or during pregnancy had a great impact on the babies' status outcome. Moreover, another contributory factor is the fact that the babies receive treatment as soon as possible after birth, mostly a single-dose nevirapine, from birth for a period of six weeks, after which the drug is replaced with cotrimoxazole. The treatment guidelines revised in 2010 stated that babies born by mothers living with HIV should receive antiretroviral therapy, go through six month breastfeeding and fed complimentarily for twelve months (20). Our research work shows prevalence is highest in babies older than six months.

The infection is transmitted to children in these age ranges via breastfeeding and the tested association was found to be statistically significant (as shown in Table 2). With a minimum 89% babies exclusively breastfed and minimum 3.5% mixed feeding (breastfeeding mixed with infant formula) across the three years reviewed (2013 to 2015), showing a 3.1% overall positivity outcome, indicates that the risk of postnatal infection, is though low in exclusively breastfed babies and high during mixed feeding, the risk is more prior to the age of 6 months, as family foods, animal milks as well as infant formula inflame and irritate the gut allowing the virus to invade the system more easily. Therefore, higher prevalence rate in babies more than 6 months is corroborated by a research work elsewhere in Western & Southern Africa (21). It is thus recommended that partial breastfeeding with complimentary food, should be in place after 6 months to enhance HIV-free child survival. In both year 2013 and year 2014, after a minimum of 6 weeks following cessation of all forms of exposure (especially breastfeeding) for babies under 18 months of age, tagged the final "early infant diagnosis of HIV in children", 288 and 204 babies were retested respectively, to know their final HIV status, with 8 (1.5%) and 5 (1.3%) babies turning out to be positive in both years respectively and referred for paediatric ARV care. Being a retrospective study, infections to these babies due to poor viral suppression could not be ascertained, as the HIV viral load, used to determine how well antiretroviral therapy (ART) is controlling the virus, could not be achieved. It is therefore recommended that mixed feeding especially within the first 6 months, should be highly discouraged. Also, a prospective cohort study is recommended and perhaps covering wider, for instance, a region of the country or the entire country, to have more revealing information about PMTCT programme.

CONCLUSION

Administration of ART to both HIV-infected mothers and their babies has demonstrated an effective mechanism of PMTCT programme, as this is evident in the low positivity outcome. However, the degree to which Cuba, Armenia, Belarus, and Thailand have eliminated HIV transmission from mother-to-baby is achievable in Nigeria, especially by scaling up the PMTCT programme thereby further increasing the access to antiretroviral drugs and applying the tactics of universal healthcare access provision to the citizenry with a focus on prevention of disease in basic health centre, as a major breakthrough in Nigeria will be a great boost in the campaign to rid the world of the virus and end the AIDS epidemic.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ondo State Ministry of Health Research.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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