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Human Immunodeficiency Virus Infection among Exposed Infants in Selected Primary Health-Care Facilities in Nigeria: A Retrospective Cohort Study

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ABSTRACT

BACKGROUND: *Nigeria is the second largest country with paediatric HIV infections. Mother to Child transmission of HIV remains a major source of paediatric infection in Nigeria. This study was conducted to determine the outcomes of HIV exposed infants in selected Primary Health Care Centres.*

METHODS: *A retrospective cohort study on HIV exposed infants between January 2015 to July 2016. A proforma was used to abstract information from clinic records on socio-demographics characteristics, ARV prophylaxis, mode of delivery, birth weight, infant prophylaxis, early infant diagnosis (EID), referral to ART. Descriptive and multivariate analysis was done to determine predictors of HIV infection among exposed infants.*

RESULTS: *170 exposed infants were recruited, and more than two-third of the infants were males (74.1%) with median age 4±3months ranging from (0 -11months). One hundred and fifty (88.2%) received infant prophylaxis and 116 (68.2%) had EID done at 6weeks. Of the 170 exposed infants 19(11.1%) were positive at 18months. Predictors of HIV infection were age of mothers ≥30years (Adjusted Odd's Ratio = 2.5,95%CI 1.9 – 16.93), Vaginal tear (Adjusted OR= 2.7,95%CI 2.1- 19.21), infants whose maternal CD4 count < 500(Adjusted OR= 3.5,95%CI 1.7 -15.02) and infant received prophylaxis other than daily Nevirapine for 6weeks (Adjusted OR=3.0,95%CI 2.4-12.74).*

CONCLUSION: *The positivity rate among studied exposed infants was high. Continuous placement of younger HIV positive mothers and exposed infants on recommended prophylaxis and timely early infant diagnosis will go a long way in reducing the burden of paediatric HIV.*

KEYWORDS: *HIV infection, Primary Health Care Centers, Exposed Infants*

INTRODUCTION

Nigeria is the second largest country with burden of HIV in the world, and around two-thirds of new HIV infections in the African region in 2017 occurred in Nigeria (1). In 2018,130,000, new HIV

infections and 53 000 AIDS-related deaths occurred in Nigeria, and 1,900, 000 people were living with HIV. Among these55% were on treatment, while only 35% of children aged 0–14 years living with HIV were on treatment (2). Among pregnant women living with HIV, 44% accessed antiretroviral medicine to prevent transmission of the virus to their baby, preventing 7200 new HIV infections among newborns. Early infant diagnosis—the percentage of HIV-exposed infants tested for HIV before eight weeks of age—stood at 18% in 2018(2).

The UNAIDS Catch-Up Plan for West and Central Africa, outlines a target to enrol an additional 140,000 children across the region on ART by 2020 (3). Reducing mother-to-child transmission remains a major target area, and Nigeria was selected as one of UNAIDS' 23 priority countries for PMTCT – being one of the nations with the highest HIV burden yet low levels of treatment coverage during pregnancy. Of these 23 countries, Nigeria has the second lowest level of ART coverage in pregnant women (4).

The numbers of children and young adults becoming infected with HIV and dying from AIDS is probably going to remain high, unless the HIV response – both prevention and treatment – improves significantly (5). The number of pregnant women visiting health facilities remains low, as does the number of health facilities providing PMTCT services, with only 7,265 health facilities providing PMTCT in 2015(6). Nigeria's major drawback is that 25% of women give birth at home or in birth homes run by traditional birth attendants, where women are unlikely to get tested for HIV (7). Despite national commitments to attain universal access to HIV prevention, treatment, care and support, many people still do not have access to the HIV services needed, especially in poor, rural areas who are majorly served by primary healthcare facilities. Regular HIV testing, treatment and care for children with HIV/AIDS can enable them to live long and have fulfilling lives. However, an absence of necessary investment and resources for adequate testing, pediatrics ARVs and children-oriented prevention programmes may make the children more prone to the consequences of the epidemic.

"Primary Health Care is essential health care based on practical, scientifically sound and socially acceptable methods and technology, made universally accessible to individuals and families in the community through their full participation and at a cost that the community and the country can afford to maintain at every stage of their development in the spirit of self-reliance and self-determination" (8). Essential health services that should be available at primary healthcare facilities in relation to HIV and AIDs are voluntary counselling and testing (VCT), basic HIV prevention and treatment for simple opportunistic infections; the provision of other HIV services at primary healthcare level, such as anti-retroviral treatment and treatment for complicated opportunistic infections.

Primary healthcare facilities should provide clear, efficient and effective referrals to higher levels of the health system for all HIV services not available, including the provision of more complex services, such as viral load testing. A primary healthcare (PHC) approach is generally considered as being central to providing equitable healthcare (9). The decentralization of care includes the provision of HIV care and treatment such as antiretroviral therapy, both in PHC clinics and within communities (10). It has been found that the integration of HIV care and treatment services in primary healthcare benefit the larger PHC system (11). Decentralization of HIV/AIDS services requires the expansion of HIV management programs including ART and PMTCT to a greater scale, with an emphasis on increasing utilization to improve the quality of life for a significant number of people living with HIV and AIDS (PLWHA) and HIV-positive pregnant women (12). Nigeria's population is served by a three-tier health service delivery system (primary, secondary and tertiary) of public and private facilities. Currently, most HIV/AIDS services are provided in the secondary and tertiary facilities managed by the public sector, which attracts most of Nigeria's health resources including qualified staff (12). This study was conducted to determine outcome of HIV exposed infants and identify predictors for this outcome in selected primary healthcare centers in Ibadan, Oyo State, Nigeria.

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MATERIALS AND METHODS

Study area: Ibadan is the capital and most populous city of Oyo State, Nigeria. With an estimated population of 3million, it is the third most populous city in Nigeria after Lagos and Kano (13). According to NACA, 200,000 persons in Oyo State are living with the Human Immuno-Deficiency Virus (HIV) and the dreaded Acquired Immune Deficiency Syndrome (AIDS), and only eight per cent of the affected persons were receiving treatment. About 10,000 expectant mothers in Oyo State are living with HIV, and about 50 people contact HIV in the state daily (1). There are twenty-one government owned health facilities in Ibadan offering PMTCT services (14). This was a retrospective cohort study conducted from April to May 2018.

Participants for this study were mother-child pairs registered in selected PMTCT clinics from 1st January 2015 to July 31St, 2016. Medical records of HIV-exposed infants and their mothers enrolled into the program were reviewed for study inclusion. To determine the sample size, a post-hoc sample size calculation was used with the following parameters: prevalence of HIV among pregnant women in Oyo state was 1.9% (15), prevalence of HIV among HIV exposed infants 8.7% (16), power of 80%, 95% confidence interval and enrolment ratio of 1. The minimum sample size calculated was 169 for mother-infant pairs and was rounded up to 170**.**

Sampling Technique: A Two-stage sampling technique was used:

Stage 1: The list of all the Primary Health Care Centers (PHCs) offering PMTCT services in Ibadan was obtained. Of the eligible facilities, 14 was selected using simple random sampling.

Stage 2: A list of HIV positive mothers enrolled in each PMTCT clinics was obtained. Records of HIV mother-infant pair between 2015 and 2016 were obtained from each facility, and the sum of client load in the 14 facilities was used as the sampling frame. Records were selected proportionately and allocated based on patients' load from each facility. Mother-infant pairs were selected using systematic sampling (the first mother-infant pair in each clinic was randomly selected afterwards every 2nd mother-infant pair was selected for the interview) until the desired sample size per facility was obtained.

Study variables: The dependent variable (main outcome) was HIV status of the exposed infants (infected, not infected). HIV status was determined using results from the 1st PCR and 2nd PCR tests as well as rapid HIV test 18 months of age. While the independent variables were categorized as maternal and infant factors. Maternal factors included mother's age, educational status, marital status, occupational status, religion, mode of delivery ARV prophylaxis during ANC, labour and delivery, disclosure of HIV status, type of ARV, counseled on infant feeding options, place of delivery, mode of delivery, antenatal care visits, gestational age at first antenatal care visit, CD4 count, WHO clinical stage at enrollment. Infant factors included age of infant enrollment at the PHC, birth weight, early infant diagnosis done at 6 weeks, receipt of infant prophylaxis and infant feeding option.

Training of research assistants and pre-test of data collection tools: Four research assistants were trained for four days by the principal investigator on the objectives of the study, data abstraction techniques and how to fill the proforma using android phones. During training, the importance of maintaining patient confidentiality was emphasized.

Pre-testing of the data collection tools was done in St Anne's Hospital, Molete, which is not part of the selected PMTCT clinics. The data collection tools and proforma were pre-tested on fifteen mother-infant pair records. Appropriate corrections were done after analyzing the pre-test result and before the actual data collection. Sections which were inconsistent, invalid and poorly constructed were reviewed and corrected.

Data collection and instrument: Data was abstracted by four trained research assistants and the investigator using android phones with Open Data kit. The data collection instrument was divided into four sections namely; facility information, ANC data, HIV diagnosis and ARV data and child data.

Data analysis: The filled proforma were checked for completeness and the fields were

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checked and validated before analysis. The primary outcome variable was categorized as "0" for HIV-negative and "1" for HIV-positive. HIV positivity rate among exposed infants was calculated as the number of HIV-positive infants divided by the total number exposed who received their final HIV test results. Final infant HIV status was determined by either a PCR or rapid HIV test as appropriate to infant's age and infant feeding option. The HIV test was considered final if the PCR was done before 18 months of age but six weeks after cessation of breast feeding or a rapid test done at 18 months of age but at least six weeks after stopping breast feeding. Descriptive statistics was computed using Epi-info Version 7.0 (17) to generate summary statistics. Frequency tables, charts, proportions and means were used to describe the data.

Bivariate analyses were done to measure association between independent variables and HIV status of exposed infants using crude odd's ratio. The $p < 0.05$ was used to determine level of statistical significance. Logistic regression model was fitted to identify factors determining the HIV status of exposed infants.

Ethical consideration: Approval for the study was obtained from the Ethical Review Committee of Oyo State Ministry of Health (Approval number AD1349/547). To ensure confidentiality of any information provided, the data collection procedure was anonymous (no name was obtained). Data collection instruments were identified only from patients' unique IDs and not by names. Study team members were trained on confidentiality of respondents' data. While no personally identifiable information was collected, the abstractors saw patient names during the abstraction process. Thus, abstractors were required to sign a confidentiality agreement. Study electronic data was password protected on principal investigators personal computer.

RESULTS

Socio-demographic and health characteristics of HIV positive mothers: Table 1 shows the socio-demographic and health characteristics of HIV positive mothers. The mean age of the mothers was 31±3SD. Most of the mothers (85.3%) delivered at ≥36 weeks and a little more than half (57.6%) of them had CD4 count < 500 copies per ml. The majority (84.7%) received ARV during the current pregnancy, and 66% were referred to ART clinic.

Table 1: Socio-demographic and Health characteristics of HIV positive mothers in selected PHCs in Ibadan Oyo State 2018.

Variable	Frequency (n=170)	Percent
Age in years		
<20	11	6.4
20-29	76	44.7
30-39	68	40.0
40-49	15	8.9
Mean age 31 ± 3SD		
Gestational age at birth(weeks)		
<36	25	14.7
≥ 36	145	85.3
Parity		
0-2	122	71.8
3-5	48	28.2
Mode of delivery		
Vaginal	104	61.2
Emergency CS	19	11.2
Elective CS	47	27.6
Vaginal Tear		
Yes	19	11.2
No	151	88.8
CD4 Count		
< 500	98	57.6
≥ 500	46	27.1
Undocumented	26	15.3
WHO Clinical Stage		
1	79	46.7
2	50	29.6
3	20	11.8
4	5	3.0
Undocumented	17	8.9
Received ARV during current pregnancy		
Yes	144	84.7
No	10	5.9
Undocumented	16	9.4
Type of ARV received(n=144)		
LAD	17	21.9
Triple	123	72.2
Undocumented	4	5.9
Referred to ARV		
Yes	112	66.3
No	30	17.8
	27	15.9
Delivery Outcome		
Alive	168	98.8
Dead	2	1.2

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Infant socio and health characteristics: Table 2 shows the socio-demographic and health characteristics of exposed infants. The median age of the infants was 4±3 months. Almost three-quarter (74.1%) of the infants were males, and the majority (91.2%) had birth weight ≥ 2.5kg. Eighty-eight percent of the infants had ARV prophylaxis while 68.2% had early infant diagnosis done at 6 weeks.

The positivity rate of exposed infants: Of the 170 exposed infants studied, 19(11.1%) were found positive to HIV.

Association between socio-demographic characteristics and infant outcomes: Table 3 shows the association between socio-demographic characteristics of mothers and infants in relation to infant outcomes. Mothers who were aged ≥30 years were more likely to have infants who will be infected with HIV, and infants with birth weight ≥ 2.5kg were less likely to be infected. Mothers who had ≥ 2children were 3 times more likely to have infant who will be HIV uninfected.

Table 2: Infant Socio-demographic and Health Characteristics (n =170).

Variable	Frequency	Percent
Age(months)		
0-3	98	57.6
4-6	32	18.9
7-9	25	14.7
≥10	15	8.8
Median age 4± 3		
Sex		
Male	126	74.1
Female	44	25.9
Birth Weight(Kg)		
< 2.5	15	8.9
≥ 2.5	155	91.1
Received Prophylaxis		
Yes	150	88.2
No	20	11.8
EID done at 6 weeks		
Yes	116	68.2
No	54	31.8
Feeding Options at 3months		
EBF	152	89.4
Formula Feeding	14	8.2
Mixed Feeding	5	2.9
Referred to ART		
Yes	15	78.9
No	4	21.1

EBF means Exclusive Breastfeeding

Table 3: Association between socio-demographic characteristics and infant outcomes

Variable	HIV infected(n=19)	OR (95%CI)	HIV uninfected(151)	OR(95%CI)
Age(years)				
< 30	5(26.4)	1	48(32.0)	1
≥30	14(73.6)	**1.8(1.52-11.93)**	103(68.0)	1.5(0.98-11.28)
Parity				
< 2	6 (31.6)	1	53(35.3)	1
≥ 2	13(68.4)	1.2(0.11-3.52)	98(64.7)	**2.5(1.81-23.01)**
Marital Status				
Single	3(15.8)	1	16(10.0)	1
Married	14(73.7)	0.4(0.14-13.21)	120(80.0)	2.8(0.34-5.29)
Others*	2(10.5)	0.5(0.15-2.18)	15(10.0)	1.3(0.28-3.53)
Birth Weight(Kg)				
< 2.5	2(10.5)	1	13(8.0)	1
≥ 2.5	17(89.5)	**0.2(0.01 -0.71)**	138(92.0)	1.1(0.11-3.52)
Sex of Infant				
Male	8(42.1)	1	103(68.7)	1
Female	11(57.9)	0.5(0.16-1.94)	48(31.3)	1.8(0.29-7.20)

*Others means co-habiting, widowed or divorce, **OR = Odd's ratio

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Association between health- related characteristics and infant outcomes: Table 4 shows the association between health characteristics and infant outcomes. Mothers who delivered at gestational age ≥36 weeks were five times more likely to have infants who will be uninfected with HIV. Infants delivered through vaginal birth were five times more likely to be infected, and infants whose mothers had vaginal tear were four times more likely to be infected.

Table 4: Association between health- related characteristics and infant outcomes

Variable	HIV infected(n=19)	AOR (95%CI)	HIV uninfected(151)	AOR(95%CI)
Gestational age(weeks)				
< 36	16(84.2)	1	25(16.7)	1
≥36	3(15.8)	0.7 (0.06 -7.47)	126(83.3)	**4.6(1.66-32.2)**
Delivery Outcome				
Alive	17 (89.5)	1	141(93.4)	1
Dead	2(10.5)	0.3(0.01-4.21)	10(6.6)	2.3(0.18-5.40)
Mode of Delivery				
Elective CS	4(21.1)	1	128(85.3)	1
Vaginal birth	10(52.6)	**5.2(2.69-31.04)**	15(10.0)	1.0(0.44-3.29)
Emergency CS	5(26.3)	0.3(0.02-3.27)	8(4.7)	2.9(0.78-9.31)
Vagina Tear				
No	15(78.9)	1	137(90.7)	1
Yes	4(21.1)	**3.7(2.5-10.21)**	14(9.3)	3.8(0.65-19.3)
Mother Received ARV				
Yes	16(84.2)	1	141(93.4)	1
No	3(15.8)	**2.2(1.7-5.32)**	10(6.6)	3.1(0.72-8.21)
EID done at 6weeks				
Yes	8(42.1)	1	108(71.5)	1
No	11(57.9)	**2.5(2.0-18.93)**	43(28.5)	0.1(0.06-1.85)
Received Infant Prophylaxis				
Yes	13(68.4)	1	141(93.4)	1
No	6 (31.6)	**1.7(1.5-15.42)**	10(6.6)	2.0(0.79-10.34)
Type of Prophylaxis received				
NVP daily for 6weeks	10(76.9)	1	145(96.0)	1
Others	3 (23.1)	**3.0(2.9 – 12.74)**	6(4.0)	1.5(0.7 -9.9)

Socio-demographic and Health predictors of outcomes of exposed infants: Table 5 shows the predictors of outcomes of exposed infants. The predictors for infants to be HIV infected were mothers who were aged ≥30years, mothers with vaginal tear during delivery, maternal CD4 count < 500, infants who did not have EID done at 6 weeks, infants who received ARV prophylaxis other than daily Nevirapine for 6 weeks with HIV.

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Table 5: Socio-demographic and Health predictors of outcomes of exposed infants

Variable	HIV infected(n=19)	AOR (95%CI)	HIV uninfected(151)	AOR(95%CI)
Age(years)				
< 30	5(26.4)	1	48(31.8)	1
≥30	14(73.6)	**2.5 (1.9-16.93)**	103(68.2)	1.5(0.98-11.28)
Gestational age(weeks)				
< 36	3(15.8)	1	25(16.7)	1
≥36	16(84.2)	0.7 (0.6 -4.74)	126(83.3)	4.6(0.60-23.2)
Parity				
< 2	6 (31.6)	1	53(35.3)	1
≥ 2	13(68.4)	1.2(0.1-5.52)	98(64.7)	**2.0(1.40-13.71)**
Birth weight (Kg)				
< 2.5	2(10.5)	1	12(8.0)	1
≥ 2.5	17(89.5)	1.1(0.11-3.52)	139(92.0)	0.2(0.11-4.71)
Maternal CD4 Count				
≥ 500	14(64.3)	1	141(93.4)	1
<500	5(35.7)	**3.5(1.7-15.02)**	10(6.6)	3.1(0.72-8.21)
Received Infant Prophylaxis				
Yes	10(53.6)	1	11(6.7)	1
No	9(46.4)	1.7(0.9-15.42)	140(93.3)	0.5(0.21-0.92)
Type of Prophylaxis received				
NVP daily for 6weeks	8(80.0)	1	145(96.0)	1
Others	2 (20.0)	**4.5(2.7-38.93)**	6(4.0)	0.1(0.06-1.85)

DISCUSSION

This study described the outcomes of exposed infants of HIV positive mothers and the predictors of this outcome. Our study revealed that the positivity rate of HIV among HIV-exposed infants in selected primary healthcare in Oyo state was 11.1%, which means one in ten exposed infants had positive status. This is still a burden to our society. A similar result was reported in Kano, Nigeria (18), Ibadan (19) and Zambia (20). However, a contrary result was reported from Nigeria in 2014 (21). This difference may be the result of different study settings and region of the country and the difference in the methodology and sample size of the two studies. Although this study was conducted in primary healthcare centers, it reiterates the fact that pediatric HIV infection is still a significant public health issue in Nigeria, and the figures indicate a need for more preventive efforts in combating the disease.

This study showed that mothers in the higher age group (≥ 30 years) were more likely to have infants who will acquire HIV infection; however, maternal age did not predict infants' HIV status. A similar study by Akinsanya et al in a primary healthcare center in South Africa

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had shown that maternal age greater than 21 years was the only significant risk factor associated with MTCT (22).

HIV is transmitted sexually when infected fluids encounter mucous membranes. Cuts or sores will increase the risk of transmission, but the risk is there without cuts, tears, or sores. The mucous membranes of the vagina experience a considerable amount of microtrauma (small tears in the vaginal wall that are not visible to the naked eye) during sex, and this microtrauma likely increases the probability of HIV transmission. The findings from this study showed that there is risk of HIV infection among infants whose mothers had vaginal tear during delivery even though no previous study has documented clear evidence on this.

Low maternal CD4 count was associated with risk of acquiring HIV infection in this study. This finding is similar with the result of a study conducted by Akinsanya et al in South Africa. A study conducted among exposed infants in Zimbabwe concluded that there was no effect of maternal CD4+ T-cell count on exposed infant morbidity and mortality (23). However, maternal CD4 cell count less than 200 cells/µl as in other studies has been associated with increased risk of all-cause infant sick clinic visits in the first year of life as cited by Athena et al. (24), possibly due to the mother's poorer health and inability to care for the infant, or other factors such as length of infant exposure to mother's pathogens or immunologic abnormalities in the HIV-exposed infants. Interestingly, a study conducted among European newborns of mothers with high and low CD4 counts concluded that mothers with high CD4 counts (> 500 cells/µl) that had taken sdNVP had significantly increased white blood cell, monocyte and basophil counts compared to newborn infants of mothers with similar CD4 counts that had not taken sdNVP; this was not evident in infants of mothers with CD4 counts <200 cells/µl. The outcome justifies the commencement of antiretroviral therapy (ART) in HIV-infected pregnant women with low CD4 count. This finding is in tandem with what previous research has shown: the lower the CD4 count of the mother, the higher the rate of vertical transmission of HIV infection. Although the risk was low for vertical transmission of HIV when maternal CD4 count is above 500, there is still a chance of MTCT.

The national guideline says that all exposed infants whose mothers are on ART should receive daily NVP from birth (or as soon as possible thereafter) until 6 weeks of age. All breastfeeding exposed infants whose mothers are not on ART should receive daily NVP from birth (or as soon as possible thereafter) until 1 week after all exposure to breast milk has ended. A cross-sectional study among exposed infants in rural Uganda reported that infants who did not receive any form of prophylaxis were nine times more likely to be HIV positive (25) which is in line with the findings of this study.

In conclusion, the level of HIV infection among HEIs in primary health care centres in Oyo state remains high. Low Maternal CD4 count, age of mothers, vagina tear and early infant diagnosis not done in the first 6 weeks were predictors for acquiring HIV infection among the study population. Adequate attention should be paid to care of exposed infants especially at the PHC levels. Continuous placement of HIV positive mothers and exposed infants on prophylaxis and timely initiation of ART will go a long way in reducing the burden of pediatric HIV.

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