

## Implications of Mother to Child Transmission of HIV among Infected Pregnant Women and their Infants attending a PMTCT ARV Clinic in Ibadan, Nigeria

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Received: 09-01-2019 / Revised: 07-03--2019 / Accepted: 15-03-2019

### Abstract

**Background:** Mother-to-child transmission (MTCT) is a major means through which HIV infected pregnant mothers pass the virus to their infants. This study aimed to assess the implications of MTCT of HIV among infected Pregnant Women and their Infants. **Methods:** 60 consenting HIV infected pregnant women attending a PMTCT ARV clinic in Ibadan, were followed up for eighteen months. Data were captured using structured questionnaire and analyzed to identify associations. **Results:** The mother's age range was 24-41 years with a mean of 32.9 years, while the infant's median age was 35 days. 32 (72.7%) of them were females with mean birth weight of 3.10 Kg. MTCT of HIV was 4.5% (2/44). Majority of the respondents were of parity 1 (22.7%) and parity 2 (27.3%) and are in monogamous marriage (81.8%), while predominant religion and occupation were Christianity (59.1%) and Trading (56.8%). Viral load was negatively correlated with hemoglobin ( $r=-0.334$ ), lymphocyte ( $r=-0.188$ ), and neutrophil ( $-0.151$ ) but positively correlated with WBC count ( $r=0.141$ ). However, between pregnancy and birth CD4 count increased from 503 to 716 ( $p<0.001$ ). Viral load at birth was higher in positive babies (Mean=4.13, SD=0.06) than negative (mean=1.18, SD=0.71) with  $p=0.001$ . **Conclusions:** This study identified high risk as predictors of MTCT of HIV among exposed infants on follow up with severe implicating consequences. Therefore, testing for pregnant women for HIV should be a national priority, hence the need for more sensitization on the utilization of PMTCT program in Nigeria.

**Keywords:** Follow-up, HIV-exposed infants, Ibadan, MTCT, PMTCT, program

### Introduction

Over 3.5 million people (3.4%) are living with HIV in Nigeria, the most populous black nation in Africa, an estimate that places the country as second with the highest burden of HIV globally [1,2].

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Also, the country has the largest number of children acquiring HIV infection—estimated at 60,000, a number that has remained largely unchanged since 2009 [3]. Furthermore, 80% of HIV infected pregnant women did not receive antiretroviral medications for PMTCT and the same 80% of women or infants did not receive ARV drugs during breastfeeding to prevent MTCT of HIV [3]. Without urgent action in Nigeria, the global target of a decline of 50% of new paediatric HIV infection projected for between 2009 and 2020 is unlikely to be achieved. In addition, sub-Saharan Africa continues to tolerate the burden of the HIV pandemic, with Nigeria as one of the countries with the

highest burdens of paediatric AIDS [4]. In 2011, the country had an estimated 440,000 children, below 15 years, living with HIV [5]. Providing ARV prophylaxis to pregnant women living with HIV and AIDS has prevented more than 350,000 children from acquiring HIV infection since 1995 resulting in a 24% decline in newly infected infants and children since 2004 [6]. This statistical data favor the implementation of PMTCT program in controlling the spread of HIV via MTCT as practiced in industrialized nations of the world [5]. Mother-to-child transmission (MTCT) of HIV can occur in uterine (in-utero), during delivery (intrapartum), after birth (postnatally) or through breastfeeding. Strategies to reduce MTCT focus on these stages of exposure which include the use of antiretroviral drugs, caesarean operation before onset of labour and total avoidance of breastfeeding the newborn [7]. These combined interventions when adhered strictly, reduce the risk of MTCT to about 1-2% [8]. However, without these interventions, about 30-45% of all infants born to HIV infected mothers will be infected and close to 10-20% will be infected via breastfeeding [9].

The national action for control of AIDS (NACA) in Nigeria has identified the challenges facing PMTCT to include poor uptake despite the availability of PMTCT services and commodities amongst others [10]. However, many Nigerians could not still access these services either due to ignorance or lack of information as regards its public health importance. The implications of inaccessibility and improper utilization of these services will be inimical to the control of MTCT of HIV among this population in Nigeria. Hence, this study was therefore designed to assess the implications of MTCT among HIV infected mothers and their exposed infants on follow up at a PMTCT ARV clinic in Ibadan, southwest Nigeria.

### Materials and methods

A follow up study was investigated among HIV infected mothers and their new born who were on enrolment at the PMTCT ARV referral clinic of Adeoyo Maternity Teaching Hospital, Ibadan, southwest Nigeria. Ethical approval for implementation of this research was taken from Oyo state ministry of health ethical review board with reference number AD13/479/795.

**Study area and design.** A total of 60 consenting HIV infected pregnant women attending a PMTCT ARV clinic in Ibadan, were followed up between September, 2015 and October, 2016. This secondary health facility is located in Northwest region of Ibadan (the second largest city in West Africa and capital of Oyo State, Nigeria). It is one of the oldest health institutions in

southwest Nigeria having an Antiretroviral (ARV) clinic which serve as a referral centre for many district hospitals in the area providing services for over 6 million people in the residing in the area and beyond. Apart from other services, the hospital provides HIV management and care in addition to PMTCT services for clients since 2001 as one component of comprehensive HIV/AIDS care and support program for AIDS Prevention Initiative in Nigeria (APIN) and PEPFAR (APIN-Plus) in Nigeria. It complements the roles of the University College Hospital, Ibadan and serves the community more than any other healthcare facility patronized by many due to many free services rendered to the grassroots supported by the State government.

### Participants and sample collection

A total consenting HIV positive pregnant women referred to PMTCT HIV clinic at Adeoyo Maternity Teaching Hospital Ibadan enrolled for the study and followed up for one year until end of term and beyond. Only 44 mother-infant pairs (attrition rate of 26.7% was recorded due to death and other unforeseen circumstances) data were analyzed. After delivery, both mothers and their infants were also captured into the ongoing program. The cohort comprised of Anti-retroviral therapy (ART) naïve and compliant pregnant women and their infants. The follow up of HIV infected mothers and their new born in southwest Nigeria PMTCT protocols according to WHO guidelines was followed over the period of the study while the international guidelines were not left out. During this study period, women who were eligible for HIV treatment based on the results of CD4 and viral load together with their clinical and immunologic status were given combination antiretroviral therapy (ART) commonly called Highly Active Antiretroviral Therapy (HAART). The ethical approval for the study was obtained from Oyo State Ethical Review Board committee of the Ministry of Health (AD13/479/795).

**Postpartum activities:** The MTCT mode for each mother-infant pair was resolved by the timing of the first HIV-1 PCR-positive test for the infant. Any infant with evidence of PCR-positive test at birth was believed to have acquired the virus in utero, while those with evidence of PCR-negative at birth and at 1 month of age and PCR-positive after 42 days (6 weeks) were believed to be infected through breastfeeding. The WHO guidelines required that the follow up schedule of infants born to HIV-positive mothers is at 6 hours after birth, 6th day and then at the 6th, 10th and 14th week of life. Afterwards, this was done on monthly basis until 6th month of age and every 3 months until age of 18 months for those infants without any symptoms. However, these infants were followed

up for uneven and ample periods of time since their HIV status could be ascertained at different period.

#### Sample collection and analysis

Blood samples were collected from all consenting HIV infected pregnant women at each visit to PMTCT ART clinic for this study. At postpartum, parental assent was obtained for the underage infants before sample collection. Demographic and other relevant information of all respondents were collected by interview before blood sample collection which included age, duration of drug usage, gestational age, HIV test result and their occupation. Venous blood sample from all the respondents was collected into plain EDTA tubes and subsequently processed for Packed Cell Volume (PCV), CD<sup>4</sup> T cells count, viral nucleic acid quantification and Molecular assays. A midwife nurse administered a structured epidemiological questionnaire to capture demographic and all other relevant information. Data were analyzed, using STATA version 12 software (StataCorp, College Station, Texas, USA) and presented as simple averages and percentages. Statistical analysis was done using the Pearson's Chi-square test and Fisher's exact test. Identified associations at  $p < 0.05$  were considered significant.

#### Laboratory analysis and assay procedures

CD4 quantification assay: CD<sup>4</sup> T lymphocyte cell was quantified using a PartecCyflow automated counter (Cyflow, Partec, Munster, Germany) within 6 hours of blood collection from all participants.

Viral load count: The assay was done using COBAS AmpliPrepTaqMan HIV -1 test version 2.0, a nucleic acid amplification test for the quantification of HIV-1 RNA in human plasma to quantify the viral load (Copies/MI). This auto analyzer uses three major processes: (i) isolation of HIV RNA; (ii) conversion of the target RNA to generate complementary DNA (cDNA) by reverse transcription and (iii) amplification of target cDNA and detection of cleaved dual-labelled oligonucleotide detection probe specific to the target simultaneously by PCR.

HIV-1 DNA-PCR test: This assay was carried out on whole blood collected from infants aged 0 to <18 months. The host DNA is extracted to detect HIV cDNA (Provirus) by amplification and detection via ELISA technique. OD value <0.2 is negative while OD

value  $\geq 0.8$  was considered positive. NB: Any infant whose HIV-1 PCR tests were negative at birth but positive after 1 month were considered to have acquired the virus either intrapartum or early postpartum.

#### Result

The mothers age range was 24-41 years with a mean of 32.9 years (SD=4.2) while the infants median age was 35 days with a range from 1 day to 228 days. MTCT of HIV was 4.5% (2/44). Distribution of their parity showed that majority were of parity 1 (22.7%) and parity 2 (27.3%). Trading (56.8%) was the commonest occupation, followed by civil service workers (18.2%). Majority of the respondent are in monogamous marriage (81.8%). Predominant religion among study participants was Christianity (59.1%). Twelve of the women have been on treatment for less than one year while 25.0% and 36.4% have been receiving treatment for 1-2 years and 3-4 years respectively. All the infants received Nevirapine (NVP) syrup at birth with the exception of 4 (9.0%) others who were delivered at home but still had access to NVP. Their sex distribution showed that 32 (72.7%) were females. The mean birth weight of the children was 3.10 Kg (SD=0.51) (Table 1).

#### Relationship/association of predictors of MTCT of HIV and their implications

Viral load was found to be negatively correlated with haemoglobin ( $r = -0.334$ ), lymphocyte ( $r = -0.188$ ), and neutrophil ( $r = -0.151$ ). In contrast, there was a positive correlation with white blood cell count ( $r = 0.141$ ). However, none of them attained statistical significance (Table 2). There was an obvious change in both parameters between pregnancy and at birth. For instance, CD4 count increased from 503 to 716 ( $p < 0.001$ ) while the Log viral load declined from 1.41 to 1.32 ( $p = 0.136$ ). The only factor found significantly different between the two groups was the Log viral load at birth which was higher in positive babies (Mean=4.13, SD=0.06) than negative (mean=1.18, SD=0.71) with  $p$ -value <0.001. Other parameters found to be higher in positive babies (though not statistically significant) include breast milk sodium, potassium, urea, and lymphocytes. Sero-negative babies had higher maternal CD4 count (before and after delivery), lymphocytes and breast milk chloride (Tables 3 and 4).

**Table 1a: Demographic description of the 44 study participants**

| Variables     | Frequency | Percentage |
|---------------|-----------|------------|
| <b>Parity</b> |           |            |
| 0             | 3         | 6.8        |
| 1             | 10        | 22.7       |

|                        |    |      |
|------------------------|----|------|
| 2                      | 15 | 34.1 |
| 3                      | 12 | 27.3 |
| 4                      | 4  | 9.1  |
| <b>Occupation</b>      |    |      |
| Artisan                | 11 | 25   |
| Civil servant/Teaching | 8  | 18.2 |
| Trading/student        | 25 | 56.8 |
| <b>Marriage type</b>   |    |      |
| Monogamy               | 36 | 81.8 |
| Polygamy               | 8  | 18.2 |
| <b>Religion</b>        |    |      |
| Christianity           | 26 | 59.1 |
| Islam                  | 18 | 40.9 |
| <b>Duration of ART</b> |    |      |
| less than 1 year       | 12 | 27.3 |
| 1-2 years              | 11 | 25   |
| 3-4 years              | 16 | 36.4 |
| >= 5 years             | 5  | 11.4 |

Table 1b: Child characteristics

| Variables                     | Frequency | Percentage |
|-------------------------------|-----------|------------|
| <b>Child's sex</b>            |           |            |
| Male                          | 12        | 27.3       |
| Female                        | 32        | 72.7       |
| <b>Birth outcome</b>          |           |            |
| Alive                         | 42        | 95.5       |
| Dead                          | 2         | 4.5        |
| <b>Nevirapine syrup given</b> | 44        | 100        |

Table 2a: Comparison of maternal CD4 count and plasma Viral Load before and after delivery

| CD4 count         | Mean  | SD    | test  | p-value |
|-------------------|-------|-------|-------|---------|
| Before delivery   | 503.2 | 199.6 |       |         |
| After delivery    | 716   | 333.7 | 3.989 | p<0.001 |
| <b>Viral load</b> |       |       |       |         |
| before delivery   | 1.41  | 0.84  | 1.518 |         |
| at birth          | 1.32  | 0.93  |       | 0.136   |

Table 2b: Correlation between antenatal plasma viral load and haematological parameters of mothers in the study

| PARAMETER | VIRAL LOAD          |         |
|-----------|---------------------|---------|
|           | PEARSON CORRELATION | P VALUE |
| WBCBD     | 0.141               | 0.361   |
| HBBD      | -0.334              | 0.027   |
| LYMBD     | -0.188              | 0.222   |
| NEUBD     | -0.151              | 0.327   |

**Key:** WBCBD: white blood cells before delivery

HBBD: haemoglobin level before delivery

LYMBD: lymphocytes count before delivery

NEUBD: neutrophil count before delivery

**Table 3: Comparison of plasma viral load with maternal background characteristics and child survival status**

| Variables              | Mean | SD   | Test statistic | p-value |
|------------------------|------|------|----------------|---------|
| <b>Parity</b>          |      |      |                |         |
| 0                      | 1.59 | 1.02 |                |         |
| 1                      | 1.31 | 0.37 |                |         |
| 2                      | 1.48 | 1.03 |                |         |
| 3                      | 1.18 | 0.45 |                |         |
| 4                      | 1.92 | 1.65 | 0.665          | 0.620   |
| <b>Occupation</b>      |      |      |                |         |
| Artisan                | 1.19 | 0.39 |                |         |
| Civil servant/Teaching | 1.39 | 0.99 |                |         |
| Trading/student        | 1.51 | 0.95 | 0.498          | 0.612   |
| <b>Marriage type</b>   |      |      |                |         |
| Monogamy               | 1.41 | 0.89 |                |         |
| Polygamy               | 1.40 | 0.65 | 0.002          | 0.962   |
| <b>Religion</b>        |      |      |                |         |
| Christianity           | 1.40 | 0.89 |                |         |
| Islam                  | 1.43 | 0.8  | 0.013          | 0.908   |
| <b>Birth outcome</b>   |      |      |                |         |
| Alive                  | 1.37 | 0.83 |                |         |
| Dead                   | 2.29 | 0.66 | 2.38           | 0.130   |

**Table 4: Maternal immunological, haematological parameters in comparison to baby's sero - status**

| Parameter                        | Positive mean (s.d) | Negative Mean (s.d) | T test | P value |
|----------------------------------|---------------------|---------------------|--------|---------|
| Cd4ad                            | 605.5 (106.773)     | 721.26 (340.485)    | 0.475  | 0.637   |
| Log viral load at birth          | 4.132 (0.063)       | 1.183 (0.713)       | -5.784 | 0.000   |
| <b>Heamatological parameters</b> |                     |                     |        |         |
| Wcbdbd                           | 5.0 (1.414)         | 6.17 (1.937)        | 0.837  | 0.407   |
| Hbbd                             | 12.5 (0.707)        | 11.0 (2.0)          | -1.047 | 0.301   |
| Lymbd                            | 36.5 (13.435)       | 42.76 (11.645)      | 0.74   | 0.463   |
| Neubd                            | 21.5 (20.406)       | 44.3 (15.133)       | 2.011  | 0.051   |
| Cdbd                             | 458 (12.728)        | 505.38 (204.155)    | 0.325  | 0.747   |
| <b>Breast milk chemistry</b>     |                     |                     |        |         |
| Na                               | 38 (1.414)          | 29.9 (3.372)        | -1.109 | 0.274   |
| K                                | 15 (1.414)          | 11.74 (37.012)      | -1.35  | 0.184   |
| Cl                               | 31 (0)              | 65.6 (3.506)        | 1.307  | 0.198   |
| Hco3                             | 6 (0)               | 8.62 (3.506)        | 1.045  | 0.302   |
| Urea                             | 62 (2.828)          | 52.05 (17.051)      | -0.816 | 0.419   |
| Lymph                            | 73.5 (3.536)        | 59.83 (26.150)      | -0.731 | 0.469   |
| Neurt                            | 26 (2.828)          | 24.79 (12.938)      | -1.131 | 0.896   |

**Key:** CDAD –cd4 count after delivery, CDBD –cd4 count before delivery, WBCBD –white blood cells before delivery,LYMBD- lymphocyte before delivery, NEUBD- neutrophil before delivery, HBBd- haemoglobin before delivery, Na-sodium, K- potassium, Cl –Chloride, HCO3- Hydrogen carbonate

## Discussion

Inaccessibility to PMTCT program and its implementations have many implications for the prevention and control of MTCT of HIV in many developing countries especially in sub-Saharan Africa. In this study, an MTCT of HIV prevalence of 4.5% was found among infants born of infected mothers. This rate is higher than 1.6% obtained for those whose mothers fully accessed PMTCT programme as opposed to 15.0% for those whose mothers had incomplete participation and 53.6% for those whose mothers did not participate [11,12]. This rate is also higher than the expected MTCT reduced risk of between 1-2% in places with the current interventions of Prevention of Mother to Child Transmission of HIV (PMTCT) [13]. Several factors have been implicated as responsible for breakthrough HIV infection from infected mothers to their young ones which include perinatal transmission, breastfeeding and some injuries sustained during and after labour, despite having well established PMTCT program [14, 15]. Our finding is also higher than what was reported in studies carried out in Anambra and Abuja which found prevalence rates of 3.6% and 2.7% respectively in mothers who had strictly adhered to the PMTCT protocol [16, 17, 18, and 19]. In this study, majority (91.0%) of the infants were delivered in our

setting as this may have some implications on the relatively high rate recorded. This finding is in concordance with variations reported by Iregbu *et al.* [20] which reported a higher overall rate of 7% while the prevalence of HIV in the exposed babies among only mother-baby pairs who received ARVs was as low as 1.3%. This is also highly comparable to the MTCT of HIV rates in high income countries such as North America and United Kingdom of less than 2% [21]. Furthermore, the prevalence in babies whose mothers were commenced on HAART during the pregnancy was (1.6%) thereby suggesting that time of commencement of maternal ARV, prior or during pregnancy, may have little or no impact on MTCT programme outcome [20]. Therefore, having some of the HIV-exposed infants delivered at home in this may have serious implications in the higher rate recorded. Moreover, the implication of providing ARV prophylaxis for the newborn infant is intended to “mop up” circulating virus that may have been transmitted in spite of maternal ARV prophylaxis or treatment; and it is expected to be given within the first 72 hours of life [22]. It has been well established that MTCT of HIV can occur during pregnancy, labour and delivery and during breastfeeding and that in the absence of any intervention; the rate of MTCT is about 15%-25% among non-breastfeeding populations in North

America and Europe and 25%-40% among breastfeeding populations in resource-limited countries [23]. However, with intervention, the MTCT rate can be reduced to as low as 2% [2, 23]. It becomes obvious that the burden of new paediatric HIV infection that will continue to occur in Nigeria and other Sub-Saharan countries are due to failure of some individuals in accessing the PMTCT interventions despite its availability. Apart from MTCT of HIV, multiple sexual partnerships have been seen as another major route of HIV transmission practiced globally especially in sub-Saharan Africa [1]. However in this study monogamy is predominantly practiced, the lower rate of MTCT recorded when compared with 67.7% in Abakiliki [18], 69.6% in Jos [16] and 30.0% reported from Enugu [17] where majority of the participants were involved in polygamy. The CD4 count, viral loads and other parameters of the mothers were evaluated to ascertain whether infection in those babies that were breastfed was as a result of poor or absent viral suppression. It has been established that the risk of HIV transmission through breastfeeding is 3 to 10 times higher among women with CD4 count < 200 cells/ml [21]. In this study however, viral load was found to be negatively correlated with haemoglobin ( $r=-0.334$ ), lymphocyte ( $r=-0.188$ ), and neutrophil ( $-0.151$ ). In contrast, there was a positive correlation with white blood cell count ( $r=0.141$ ) with no statistical significance. Moreover, there was an obvious change in both parameters between pregnancy and at birth. For instance, CD4 count increased from 503 to 716 ( $p=0.001$ ) while the Log viral load declined from 1.41 to 1.32 ( $p=0.136$ ). This therefore agrees with immune response to therapy of an HIV infected person responding well to antiretroviral therapy management [13]. In fact, the earlier realization of this link was part of the basis for the use of ARV drugs to lower maternal HIV viral load during pregnancy, labour and delivery [14]. Also, John and Kreiss [24], as well as Mofenson *et al.* [25] in the early 1990s linked high levels of

maternal viral HIV RNA to a higher risk of MTCT of HIV. Among many parameters which may or may not link viral load with MTCT of HIV, the only factor found significantly different between the two groups was the Log viral load at birth which was higher in positive babies (Mean=4.13, SD=0.06) than negative (mean=1.18, SD=0.71) ( $p=0.001$ ). This also agrees with the findings of Iregbuet *al.* [20] which reported similar scenario. Nevertheless, religion plays a vital role in reaching the public about the institution of PMTCT program in Nigeria but this medium has not been well utilized effectively. In this study, more than half of the participants are Christians (59.1%) and predominant occupation as traders (56.8%) who could easily embrace the ideology [26]. Through effective and comprehensive counselling and public sensitization on the PMTCT utilization, it is expected that with urgent action in Nigeria, the global target of a 50% decline of new pediatric HIV infections, set for between 2009 and 2020 [2,27] will likely to be achieved.

### Conclusion

The implications of non-utilization and inaccessibility of PMTCT programmes instituted in Nigeria to control MTCT of HIV among mothers-infants pairs will have dire consequences if urgent steps are not taken to sensitize the public on its importance. A relatively high rate of MTCT found in this study calls for urgent attention by the health authorities with a warning that Nigeria is rated 2<sup>nd</sup> after India with burden of HIV globally. The intervention in PMTCT programmes provides both mother and child the opportunity to receive adequate therapy and reduction of MTCT HIV. Therefore, testing for pregnant women, youth and children at risk of HIV should be a national priority. Determination of the effect of these specific interventions is achievable if everyone embraces this task.

### Acknowledgments

We wish to express our heartfelt gratitude to all the participants as well as the management and staff of the PMTCT ARV Centre used to carry out this work for their mutual cooperation while thanking the Oyo State Ethical Review Board for granting the study approval.

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**Conflict of Interest: None**

**Source of Support: Nil**