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# Paediatric HIV treatment outcome in Lagos: The Nigerian Institute of Medical Research experience

**David AN, Salako AO, Gbaja-Biamila TA*, Odubela OO, Opaneye BA, Wapmuk AE, Ezemelue PN and Musari-Martins TE**

Clinical Sciences Department, Nigerian Institute of Medical Research, Lagos, Nigeria

## Abstract

**Introduction:** There are several measures towards reducing the burden of paediatric HIV/AIDS globally. However, Sub-Saharan Africa and most importantly Nigeria account for a significant burden of children living with HIV with approximately a quarter of the children being on ARTs.

In order to end the Paediatric HIV epidemic, there is need to continue to evaluate the treatment outcome, so as strengthen existing measures and develop new effective strategies. This study aimed to review the treatment outcome of children enrolled at the Nigerian Institute of Medical Research [NIMR] HIV treatment and care centre in Lagos.

**Methodology** : A retrospective study design to evaluate, treatment outcomes among children living with HIV who had received care between 2006 and 2017 at NIMR a foremost quaternary health care centre and pacesetter in the management of, and research into HIV. Detailed information on the children was retrieved from the electronic medical records of the HIV care centre over a 12 year period [January 2006-December 2017]. Data obtained were analyzed using the statistical package for social science [SPSS] version 22.0.

**Results:** A total of 1,079 children were enrolled in care over the twelve-year period with a M: F ratio of1.1:1, 62.9% of the cases were children aged 0-4 years and 64.7% of the children presented with WHO stage 1&2 disease state. At the end of the review perioc, 508 (47.1%) remain in care, while 33.8% and 6.8% of the children enrolled were lost to follow-up and dead respectively. Unfavorable outcome was characterized by malnutrition, anaemia (Hb < 11.0 g/dL), WHO Stage 4 disease, HIV RNA viral load ≥ 100,000 copies/ml and Hepatitis co-morbidity at enrollment.

**Conclusion:** In children with HIV in Lagos, Nigeria, malnutrition, anaemia and advanced disease stage at presentation are associated with an unfavorable outcome. Loss to follow up remains a significant concern and every effort should be made to track and retain children in care for optimal outcome.

## Introduction

Paediatric human immunodeficiency virus (HIV) infection is of global concern with approximately 1.7 million [1.3-2.2 million] children living with HIV worldwide. Ninety percent of the affected children residing in sub Saharan Africa [1].

Several measures have been initiated to reduce the burden of paediatric HIV/AIDS; This includes increased coverage of prevention-of-mother-to child-transmission [PMTCT] [provision of ARTs to pregnant &breastfeeding mothers, Nevirapine prophylaxis for perinatal exposed newborns] [2], increased availability and accessibility of antiretroviral therapy [ART] to children living with HIV [3]. Other measures include integrating HIV care services into the algorithm of primary and secondary level of care in the country [4], among other survival and health promoting strategies. These efforts combined with improved adherence has contributed to achieving virological suppression as well as reduce the burden of paediatric HIV.

Nigeria has the second largest HIV epidemic in the world and one of the highest rates of new infection in sub-Saharan Africa. An estimated 220,000 children (0-14 years) living with HIV and about 1.8 million children were orphaned by AIDS, with far reaching devastating impact on health, safety and well-being of the Nigerian populace, with vertical transmission being the commonest route of HIV acquisition in children [5]. Strengthening the PMTCT programme has been shown to significantly reduce new paediatric HIV infections to almost zero, however, Nigeria still has the highest burden of childhood HIV and approximately only 26% are on ART treatment [6].

In order to attain the 90:90:90 goal of HIV care set by UNAIDS in 2014 [5], there is a need to review the treatment outcome of the paediatric HIV in the country. This would assist in the process of strengthening existing measures and developing new and effective strategies to end the Paediatric HIV epidemic.

This study aims to determine the treatment outcome of children enrolled in the NIMR HIV treatment and care centre in Lagos.

## Methodology

**Study design:** A retrospective cohort study design to evaluate the treatment outcomes among children living with HIV who had received care between 2006 and 2017.

**Study setting:** The data was collected from the data base of the clinical sciences department of the Nigerian Institute of Medical Research [NIMR]. Nigerian Institute of Medical Research is a foremost quaternary health care centre and pacesetter in the management and research into HIV care in Nigeria. The HIV care and management started at NIMR in 2002 but the Paediatric HIV care services started in 2004. The institute has since then been at the fore front of channeling the path for the care of people living with HIV.

***Correspondence to:*** Gbaja-Biamila TA, Clinical Sciences Department, Nigerian Institute of Medical Research, Lagos, Nigeria, E-mail: titigbajabiamila@yahoo.com

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The electronic medical data base of all enrolled HIV infected children between January 2006 and December 2017 were reviewed. Data extracted included sex, age at HIV diagnosis, socio-economic class, parental HIV status, orphan status and clinic outcomes (still in care, dead or lost to follow up (LTFU), referred/transferred out).

Treatment Outcome could be classified as favourable or unfavourable. Favourable outcome was defined as children still in current care while unfavourable outcome was defined as children who had died or been lost to follow up. The children who were transferred out and with voluntary withdrawal were excluded from analysis of treatment outcome. Lost to follow-up was defined as children who failed to return back to care after 6 months of first visit.

**Study population:** All HIV-infected children below 15 years of age who were enrolled into the program from 2006 and followed up to 2017 were included in the analysis.

**Data analysis:** Retrieved data were analyzed using the Statistical Package for Social Sciences (SPSS) version 22.0. Descriptive statistics (mean and median) were used to summarize quantitative variables (age of study participants, age at HIV diagnosis). Student t-test and Analysis of Variance (ANOVA) were used to compare the means of continuous variables while Chi-square and Fisher's exact tests were used to test for significant association of categorical variables. All statistical tests where p-value was less than 0.05 considered statistically significant.

## Results

### Social-demographic characteristics

A total of 1,079 children were enrolled within the 12 year period (2006-2017), out of which 558 (51.7%) were males while 521 (48.3%) were female. Majority of children enrolled were between the age 0-4 years (62%), were in the lower socioeconomic classes of 3-5 (75.4%) and both parents alive (65.7%). There was a decreasing trend of enrollment over the study period (Figure 1) (Table 1).

### Clinical and laboratory characteristic at enrollment

At enrollment,majority of the children were at WHO clinical stages 1 and 2 (64.7%), with viral load ≥100,00 copies/ml (58.4%), CD4 lymphocyte count ≥ 500 cells/mm$^3$ (58.5%), and haemoglobin {Hb} less than 11 g/dl (83.4%) (Table 2).

### Enrollment characteristic with respect to age group

Children aged ≥ 5-years were significantly more likely to be from lower socioeconomic class, orphaned, present with more severe disease (HIV RNA VL ≥ 100,000 copies/ml, and CD4 count less than 500 cells/μL), while children aged ≤ 4-years were significantly more likely to present with anaemia (Hb < 11 g/dL). There was no significant difference in level of disease severity [viral load, CD4] and nutritional status among the children (0-4) year and (5-14) year age groups. However, children aged 10-14 years (adolescents) were significantly more likely to be undernourished, enrolled in severe disease state compared to those aged 5-9 years (OR 2.4 [95% CI = 1.5 - 2.7], p = 0.0001 and OR 2.9 [95% CI = 1.4 - 6.1], p = 0.003 respectively). Adolescents were also significantly more likely to present with severe disease compared to younger children aged less than 5 years (OR 2.0 [95% CI = 1.0-3.8], p = 0.04 (Tables 3 and 4).

### Outcome of children enrolled

As at the end of December 2017; 47.1% were in care, while 120 (10.6%), 74 (6.8%), 12 (1.1%), and 365 (33.8%), have been transferred, died, requested voluntary withdrawal and lost to follow up (LTFU) respectively (Figure 2).

One hundred and fourteen of the 120 children were transferred to other centres while 6 (5%) were adopted outside the country. Seventy-five of the 508 children in care have transited to the adult ART service of our facility.

Table 5 depicts the outcome of enrolled children was broadly classified as favourable or unfavourable. Unfavourable outcome was associated with malnourished status, anaemia (Hb< 11.0 g/dL), WHO stage 4, HIV RNA viral load ≥ 100,000 copies/ml and Hepatitis co-morbidity.

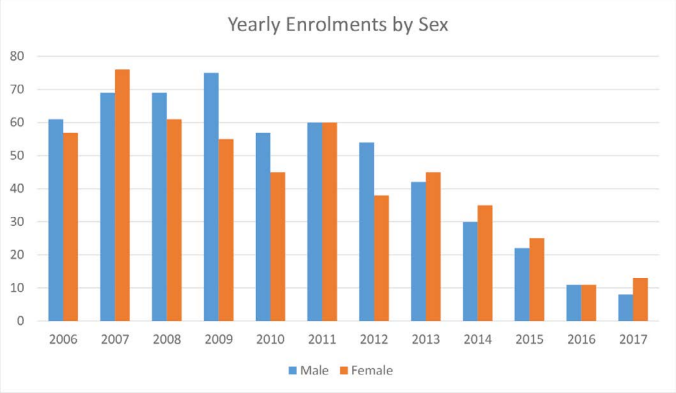


**Figure 1.** Pattern of children enrollment over 12 years

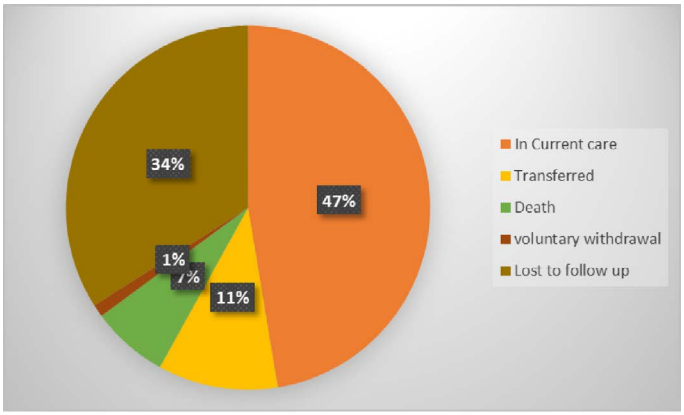


**Figure 2.** Treatment outcomes

**Table 1.** Socio-demographic characteristics of children enrolled

| CHARACTERISITICS | FREQUENCY n (%) N=1079 |
|---|---|
| **AGE DISTRIBUTION [YEARS]** | |
| **0-4** | 679 (62.9%) |
| **5-9** | 267 (24.8%) |
| **10-14** | 133 (12.3%) |
| **GENDER** | |
| **MALE** | 558 (51.7%) |
| **FEMALE** | 521 (48.3%) |
| **MALE: FEMALE RATIO** | 1.1:1 |
| **SOCIO-ECONOMIC CLASS [PARENTS]** | |
| **I & II** | 266 (24.6%) |
| **III** | 416 (38.6%) |
| **IV & V** | 397 (36.8%) |
| **ORPHAN STATUS** | |
| **Double** | 71 (6.6%) |
| **Maternal** | 183 (17%) |
| **Paternal** | 116 (10.7%) |
| **Both Parents Alive** | 709 (65.7%) |

**Table 2.** Clinical and laboratory characteristics of enrolled children

| Characteristic | Frequency (%)/Median (IQR) |
|---|---|
| **WHO Clinical Stage:** | |
| **Median (IQR)** | 2 (2-3) |
| **WHO Stage Groups:** | |
| **1 & 2** | 348 (64.7) |
| **3 & 4** | 190 (35.3) |
| **Total** | **538 (100.0)** |
| **Viral Load (copies/ml):** | |
| **Median (IQR)** | 158,054 (23,701-572,050) |
| **VL Groups:** | |
| **<100,000** | 278 (41.6) |
| **≥100,000** | 390 (58.4) |
| **Total** | **668 (100.0)** |
| **CD4 Count (cells/µL):** | |
| **Median (IQR)** | 613 (316.5-10618.5) |
| **CD4 Groups:** | |
| **<500** | 381 (41.5) |
| **≥500** | 538 (58.5) |
| **Total** | **919 (100.0)** |
| **CD4 %:** | |
| **Median (IQR)** | 15.8 (9.2-24.5) |
| **CD4% Groups** | |
| **<15%** | 345 (46.4) |
| **≥15%** | 398 (53.6) |
| **Total** | **743 (100.0)** |
| **Hb (g/dL):** | |
| **Median (IQR)** | 9.5 (8.5-10.5) |
| **Hb Groups:** | |
| **<11** | 826 (83.4) |
| **≥11** | 164 (16,6) |
| **Total** | **990 (100.0)** |
| **Hepatitis Coinfection:** | |
| **HBV** | 23/555=4.1% |
| **HCV** | 10/542=1.8% |

**Table 3.** Enrollment characteristics with respect to age

| Characteristic | Age Group (years) | | OR (95% CI) | P value |
|---|---|---|---|---|
| | 0 – 4 | 5 – 14 | | |
| Sex: | | | | |
| Male | 362 (53.3) | 196 (49.4) | 1.2 (0.9 – 1.5) | 0.17 |
| Female | 317 (46.7) | 204 (50.6) | | |
| Total | **679 (100.0)** | **400 (100.0)** | | |
| Socioeconomic Class: | | | | |
| I & II | 54 (29.7) | 11 (13.9) | 2.6 (1.3 – 5.3) | 0.007 |
| III - V | 128 (70.3) | 68 (86.1) | | |
| Total | **182 (100.0)** | **79 (100.0)** | | |
| Orphan Status: | | | | |
| Yes | 42 (22.7) | 51 (54.2) | 0.2 (0.1 – 0.4) | <0.0001 |
| No | 143 (77.3) | 37 (45.8) | | |
| Total | **185 (100.0)** | **88 (100.0)** | | |
| Nutritional Status: | | | | |
| Well nourished | 390 (64.6) | 263 (69.6) | 0.8 (0.6 – 1.0) | 0.10 |
| Undernourished | 214 (33.4) | 115 (30.4) | | |
| Total | **604 (100.0)** | **378 (100.0)** | | |
| WHO Disease Stage: | | | | |
| 1 & 2 | 134 (52.3) | 79 (53.7) | 0.9 (0.6 – 1.4) | 0.78 |
| 3 & 4 | 122 (47.7) | 68 (46.3) | | |
| Total | **256 (100.0)** | **147 (100.0)** | | |

**Table 4.** Enrollment characteristics with respect to age

| Characteristic | Age Group (years) | | OR (95% CI) | P value |
|---|---|---|---|---|
| | 0 – 4 | 5 – 14 | | |
| HIV RNA VL (copies/ml) : | | | | |
| <100,000 | 141 (34.9) | 137 (51.9) | 0.5 (0.4 – 0.7) | <0.0001 |
| ≥100,000 | 263 (65.1) | 127 (48.1) | | |
| Total | **404 (100.0)** | **264 (100.0)** | | |
| CD4 Count (cells/µL): | | | | |
| <500 | 153 (27.1) | 228 (64.4) | 0.2 (0.2 – 0.3) | <0.0001 |
| ≥500 | 412 (72.9) | 126 (35.6) | | |
| Total | **565 (100.0)** | **354 (100.0)** | | |
| Hb (g/dL): | | | | |
| <11 | 535 (87.0) | 291 (77.6) | 1.9 (1.4 – 2.7) | 0.0001 |
| ≥11 | 80 (13.0) | 84 (22.4) | | |
| Total | **615 (100.0)** | **375 (100.0)** | | |

**Table 5.** Outcome of enrolled children

| Characteristic | Favourable | Unfavourable | OR (95% CI) | P value |
|---|---|---|---|---|
| **Sex:** | | | | |
| **Male** | 270 (52.5) | 224 (51.1) | 1.1 (0.8 – 1.4) | 0.67 |
| **Female** | 244 (47.5) | 214 (48.9) | | |
| **Total** | **514 (100.0)** | **438 (100.0)** | | |
| **Age Group (years):** | | | | |
| **0- 4** | 316 (61.5) | 282 (64.4) | 0.8 (0.6 – 1.1) | 0.15 |
| **5 - 9** | 141 (27.4) | 101 (23.1) | | |
| **10 -14** | 57 (10.1) | 55 (12.5) [Ref] | | |
| **Total** | **514 (100.0)** | **438 (100.0)** | | |
| **Socioeconomic Class:** | | | | |
| **I & II** | 49 (24.4) | 17 (25.4) | 0.9 (0.5 – 1.8) | 0.87 |
| **III - V** | 152 (73.6) | 50 (74.6) | | |
| **Total** | **201 (100.0)** | **67 (100.0)** | | |
| **Orphan Status:** | | | | |
| **Yes** | 69 (32.4) | 19 (30.2) | 1.1 (0.6 – 2.0 | 0.74 |
| **No** | 144 (67.6) | 44 (69.8) | | |
| **Total** | **213 (100.0)** | **63 (100.0)** | | |
| **Nutritional Status:** | | | | |
| **Well nourished** | 328 (71.1) | 232 (58.0) | 1.8 (1.3 – 2.4) | <0.001 |
| **Undernourished** | 133 (28.9) | 168 (42.0) | | |
| **Total** | **461 (100.0)** | **400 (100.0)** | | |
| **WHO Disease Stage:** | | | | |
| **1 - 3** | 188 (95.9) | 141 (87.0) | 3.5 (1.5 – 8.1) | 0.002 |
| **4** | 8 (4.1) | 21 (13.0) | | |
| **Total** | 196 (100.0) | 162 (100.0) | | |
| **HIV RNA VL (copies/ml) :** | | | | |
| **<100,000** | 148 (45.7) | 94 (36.4) | 1.5 (1.0 – 2.1) | 0.02 |
| **≥100,000** | 176 (53.3) | 164 (63.6) | | |
| **Total** | **324 (100.0)** | **258 (100.0)** | | |
| **CD4 Count (cells/µL):** | | | | |
| **<500** | 185 | 154 | 0.8 (0.6 – 1.1) | 0.13 |
| **≥500** | 277 | 185 | | |
| **Total** | **462 (100.0)** | **339 (100.0)** | | |
| **CD4%:** | | | | |
| **<15** | 169 (45.1) | 146 (48.0) | 0.9 (0.7 – 1.2) | 0.44 |
| **≥15** | 206 (54.9) | 158 (52.0) | | |
| **Total** | **375 (100.0)** | **304 (100.0)** | | |
| **Hb (g/dL): <10** | 293 | 237 | 0.7 (0.5 – 0.9) | 0.01 |
| **≥10** | 211 | 120 | | |
| **Total** | **504 (100.0)** | **357 (100.0)** | | |
| **HIV/Hepatitis Comorbidity:** | | | | |
| **Yes** | 12 (4.3) | 19 (8.8) | 0.4 (0.2 – 0.9 | 0.04 |
| **No** | 269 (95.7) | 197 (91.2) | | |
| **Total** | **281 (100.0)** | **216 (100.0)** | | |

## Discussion

In this 12-year review, the age and sex distribution of paediatric HIV in this study did not differ from previous works with children aged ≤ 5 years and male commonly affected [7-11]. This finding could be explained by the rapid progression of HIV in younger children and therefore children are more likely to be enrolled into care after they have developed AIDS [12].

The reduced client enrollment at the centre over the years is in keeping with the declining incidence of HIV in Nigeria and globally [5,13]. This could also a reflection of decentralization of care for people living with HIV as more centres are now equipped with capacity for management of HIV in children, in addition to the effectiveness of the prevention of mother-to-child transmission [PMTCT] programs among other initiatives implemented towards combating the scourge of HIV/AIDS.

At enrollment the median laboratory parameters were haemoglobin level, viral load and CD4 count of 9.5 g/dl, 158,054 copies/ml and 613 cells/µl respectively. These features at entry are understandable because most children are commonly brought into clinic when symptoms and signs are present. This is in conformity with previous works in Africa and beyond [8,9,14]. Although our centre provides essentially outpatient services, other facilities with in-patient paediatric HIV services have reported appalling clinical and immunological manifestations [7,10,11,15].

The low haemoglobin levels in children predominantly those below 5 years at presentation is in unison with prior reports depicting anaemia as a common haematological manifestation in HIV/AIDs irrespective of age in resource-limited setting [16,17]. The association between low socioeconomic class, orphan children and severe disease is in concordance with previous findings [18-21]. This buttresses the bidirectional association between HIV and socio-economic class; HIV/AIDS is submerged within social and economic inequity with high burden among children, families and societies with low socio-economic status. The individual or families in the low socio-economic background have limited access to health information including HIV care services among other challenges facing them [22-24]. Furthermore, the socio-economic status remains a key factor in predicting the quality of life and outcomes of people living with the disease.

Delayed diagnosis and presentation in severe disease state among the adolescents in this study is in concordance with report from previous studies [25,26]. In addition, challenges with acceptance of their HIV status, the need for life long ART treatment and the questionable prospect of future outcomes with respect to their health, education, social and relationship status remains an evolving obstacle for adherence to care [27].

The retention of children in our facility was 47.1%, this low retention rate could be alluded to the absence of in-patient services. Other reasons include the multi-centre diversity of HIV care in Lagos and decentralization policy on HIV treatment. However, the present retention rate is low compared to 65.3% reported by Ubesie *et al.* [28] in South East Nigeria, 56% by Mutanga *et al.* [29] in Zambia, 84.7% - 94.8% [30] in Uganda and 78-96% reported by McNairy *et al.* [31] in a four country national review involving Kenya, Mozambique, Rwanda and Tanzania. The retention rate in these facilities were alluded to the robust and comprehensive nature of their services, presence of technical support and the adoption of a general model by the countries evaluated.

The magnitude of loss to follow-up [LTFU] 33.8% is reflective of our low retention rate. The clinical outcomes of these children are unknown, though a significant proportion of the client might have moved close to their residence during the decentralization process or an ample proportion of the children might actually be dead considering the associated characteristics of anaemia, severe HIV disease (WHO Stage 4) and co-morbidities. Contact tracing was not successful to ascertain reasons why the children defaulted from care. The finding in this review is in concordance with 2.6-57% recorded by Zurcher *et al.* [32] in an extensive review in sub- Saharan Africa. However, our finding is higher compared to 23.7% reported by Ubesie *et al.* [28] in Southeast Nigeria and 22% by McNairy *et al.* [31] in a review of four other African countries receiving support from ICAP. While McNairy *et al.* [31] alluded low LTFU rate to the robust nature of the program in a small population of children living with HIV; thus ensuring time for active patient follow-up. Ubesie *et al.* [28] claimed low LTFU could be a direct reflection of the population of client reviewed (555 children living with HIV) which was lower compared to our centre. On the contrary a higher LTFU rate of 50% was reported by Yu *et al.* [33], in Malawi, though within reported attrition LTFU rates across sub Saharan Africa with death being the major reason for the high rate upon contact tracing of the children.

The attrition due to confirmed death is approximately 7% in the present 12-year review. The reason for the low mortality rate reported by our centre could be because our services are essentially out-patient care, thus, the high incidence of children LTFU whom the primary cause could have been to death could not be ascertained. This finding is in consonance with mortality trends of between 5-7% documented by Mutanga *et al.* [29] in Zambia, McNairy *et al.* [31] in a four nations' review, Brophy *et al.* [34] in Malawi and by Ahmed and Lemma [35] in a systemic review and meta-analysis of mortality among paediatric patients in sub-Saharan Africa. However, a higher death rate of 18.2% was reported in Kano Northern Nigeria by Obiagwu *et al.* [7] whom the children living with HIV at enrollment were predominantly in-patient with worse clinical presentations. Furthermore, in this current study the mortality burden of 7% is in discordance with 4.2% documented in Southeast Nigeria over a 10-year review, [29] The reason for the variance could be alluded to the reduced number of children living with HIV in the report from Southeast Nigeria.

The transfer of children living with HIV from our centre is a reflection of the plethora of available HIV care centres in the Lagos environs. In addition to the ongoing decentralization of care for people living with HIV, more centres are equipped with capacity for management of HIV in children and the relocation of caregiver for variable reasons. However, the number of children transferred out of care in our centre is higher when compared to 6.8%, 9%, by Ubesie *et al.* [28] in Southeast Nigeria in a 10-year review and Minn *et al.* [36] in Myanmar in a 12-year cohort analysis respectively. Although, higher transfers [20%] were reported in Zambia by Mutanga *et al.* [29], the reason alluded to this transfers were because the nations' Ministry of Health has a policy that encourages people to seek care at the closest health facility to their homes.

## Conclusion

In conclusion, the review shows a reduction in the prevalence of HIV over the years with low retention of children in care and a significant proportion of children transferred out of care to other centres. LTFU remains a challenge in the care of children living with HIV.

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