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Treatment Outcome of Human Immunodeficiency Virus Infected Children: A Retrospective Cohort Study in a Private Hospital in Nigeria

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Abstract

Background: The pandemic of Human Immunodeficiency Virus (HIV) and Acquired immunodeficiency syndrome (AIDS) has reversed many of the health and developmental gains over the past three decades, especially in low income countries. This study assessed the treatment outcome of HIV-infected children after two years on highly active antiretroviral therapy (HAART) in a private health facility in Benue State, North-Central Nigeria. *Methodology:* A retrospective study was employed to review the clinical records of HIV-infected children from January 2004 to December 2014. Data obtained was analysed with Statistical packages for social sciences (SPSS) version 20.0. Chi-square ($\chi 2$) test was used for test of association between the independent variables and the main outcomes of the study, with P value set at 0.05. *Results:* One hundred and one children were initiated on HAART within the period. The mean age of the patients was 8.5±3.0 years. Majority (43.6%) of those initiated on HAART had World Health Organization (WHO) clinical stage 2 disease while 63.4% were on cotrimoxazole prophylaxis. Ten (9.9%) were lost to follow up, 4.0% were transferred to a tertiary health facility while 2.0% died. Overall patients with baseline CD4 count of >350 cell/mm^3 and those with WHO stages 1 and 2 disease had higher rates of survival after two years on HAART. *Conclusion:* With prompt access to Antiretroviral Therapy (ART0 majority of HIV-1 infected children diagnosed early can now reach adulthood.

Keywords

Paediatrics, HIV, ART, Outcome, Private Hospital, Nigeria

1. Introduction

Globally, the pandemic of Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) has continued to constitute serious health and socioeconomic challenges for more than two decades. In underdeveloped and developing countries, it has reversed many of the health and developmental gains over the past three decades as reflected by indices such as life expectancy at birth and infant mortality rate among others. [1] The epidemic has also facilitated the re-emergence of disease conditions such as pulmonary tuberculosis and other opportunistic infections. It is estimated that 2.9 million children were living with HIV/AIDS in 2012. [2] In 2010, Nigeria had about 440,000 children below the age of 15 years living with HIV/AIDS and many of them were placed on highly active antiretroviral therapy (HAART). [3] One of the significant impact of HAART is the reduction in childhood morbidity and mortality.[4-8] Some of the constraints faced in initiating HAART in children include delay in early infant diagnosis and getting CD4 results. Co-infection with tuberculosis (TB) is also a constraint because of the difficulty in making a diagnosis of TB in children. Other constraints

encountered in the management of HIV infection in children are monitoring and retention in care. In this study we looked at the treatment outcome of HIV-infected children after two years on HAART in a private health facility in North-Central Nigeria.

2. Materials and Methods

The study was carried out in the Paediatric Clinic of Madonna Hospital, a private health facility in Makurdi, Benue State, Nigeria. The hospital is situated in the central area of the state capital. It provides health care services for people within Makurdi and also acts as referral centre for health facilities in the neighboring local government areas of the state. The hospital has a bed capacity of fifty-two and staff strength of two consultants, four medical officers, twenty nurses/midwives and thirty other auxiliary staff. The hospital offers specialist care in Paediatrics, internal medicine, surgery, and obstetrics and gynaecology. Other services offered include radiology, ultrasonography, blood transfusion services, counselling and screening. The hospital is also a Global Fund site for antiretroviral therapy (ART) services.

A retrospective cohort study of all available data of HIV sero-positive children aged 18 months to 15 years who were initiated on HAART in the hospital was employed for the survey. The period under review covers from January, 2004 to December, 2014. All HIV-infected children whose parents consented for ART and were registered for HAART were the cohorts for the study. However all HIV sero-positive children on HARRT with incomplete records were excluded. In total, 123 patients' records were reviewed, of which 22 were excluded in line with the exclusion criteria.

Baseline information retrieved were the socio-demographic characteristics of the patients, WHO clinical staging at commencement of ART and cotrimoxazole prophylaxis. Main outcome parameters evaluated for this study were the two years' post treatment CD4 count of the patients and their follow-up status. The follow-up status includes: alive and retained in care, transferred to another health facility, lost to follow up (LTFU), and died.

All analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 20. Data sorted were categorized, summarized, and presented in exploratory formats as frequency tables. Chi-square ($\chi 2$) test was used for test of association between the independent variables and the main outcomes of the study, with statistical significance set at P value of 0.05.

3. Results

3.1. Baseline Characteristics of Patients

The age and sex of the patients and the baseline clinical stage, CD4 count and history of cotrimoxazole prophylaxis are summarized in table 1. Of the total 123 case files reviewed, 101 (82.1%) had complete information that met the objectives of the study. The patients were between 2-15 years of age. The modal age group was 5-10 years (65.3%), followed by 11-15 years (26.7%) while 4 years and below constituted the least (7.9%). The mean age of the patients was 8.5 years (SD= ±3.0 years). Overall, the proportion of males seen in the facility over the review period was higher than the females (60.4% and 39.5% respectively). Majority (43.6%) of the patients initiated on ART had WHO clinical stage 2 disease, followed by those in stage 3 (34.7%), stage 1 (19.8%), while the least (2.0%) were the patients in stage 4. Sixty-four (63.4%) of the patients had CD4 count of >350 cells/mm3 while 37 (36.6%) had CD4 counts of and ≤350 cells/mm3. More than two-third (68.3%) of the patients were on cotrimoxazole prophylaxis throughout the period they were on ART regimen.

Table 1. *Patients baseline information (n=101).*

Variable	Male(n=61)	Female(n=40)	Total
Age (years)	**Frequency (%)**	**Frequency (%)**	**Frequency (%)**
< 5	3(4.9)	5(12.5)	8(7.9)
5-10	44(72.1)	22(55.0)	66(65.3)
11-15	14(23.0)	13(32.5)	27(26.7)
WHO clinical staging			
1	11(18.0)	9(22.5)	20(19.8)
2	24(39.3)	20(50.0)	44(43.6)
3	26(42.6)	9(22.5)	35(34.7)
4	0(0.0)	12(5.0)	2(2.0)
CD4 count (cells/mm^3)			
≤350	22(36.1)	15(37.5)	37(36.6)
>350	39(63.9)	25(62.5)	64(63.4)
Cotrimoxazole prophylaxis			
Yes	44(72.1)	25(62.5)	69(68.3)
No	17(27.9)	15(37.5)	32(31.7)

3.2. Outcome After 2 Years on ART

The summary of the follow-up status and CD4 count by gender stratification of the patients is shown in Table 2. Fifty-two (85.2%) of the males were alive and retained in care, 6(9.8%) were lost to follow-up, 3 (4.9%) were transferred to a tertiary health facility while none died. Thirty-three (82.5%) of the females were alive and retained in care, 4(10.0%) were lost to follow up, 1 (2.5%) were transferred while 2 (2.0%)

died. All the recorded deaths were females and they constitute 2.0% of the overall patients. Forty (65.5%) males and 31 (77.5%) females had CD4 count of >350 cells/mm^3 after two years of ART. Overall 71 (70.3%) of the patients had CD4 count of >350 cells/mm^3 after two years on HAART.

Table 2. *Patient's follow-up data.*

Outcome Variable	Frequency (%)		
Follow-up	**Male**	**Female**	**Total**
Alive and retained in care	52(85.2)	33(82.5)	85(84.2)
Lost to follow up	6(9.8)	4(10.0)	10(9.9)
Transferred	3(4,9)	1(2.5)	4(4.0)
Died	0(0.0)	2(5.0)	2(2.0)
CD4 Count (Cells/mm^3)			
≤350	18(29.5)	7(17.5)	25(14.8)
>350	40(65.6)	31(77.5)	71(70.3)
Not done	3(4.9)	2(5.0)	5(5.0)

Tables 3 shows the relationship between the independent variables and patients' outcome.

Lost to follow up was more common amongst patients aged 11-15 years followed by those aged <5 years. The proportion of patients with CD4 count of >350 cell/mm^3 was lowest amongst patients aged 11-15 years. However, the relationship between the age of the patients and the two years' post treatment CD4 count or follow-up status of patient was not statistically significant (p= 0.378 and p=0.141 respectively). The proportion of females with CD4 count >350 cells/mm^3 after two years of treatment was higher than the males; however the difference was not statistically significant (p= 0.387).

Nineteen (95.0%) of patients in WHO clinical stage 1 had CD4 count >350 cells/mm^3, compared to 30 (68.2%) of those in stage 2 and 21 (60.0%) of those in stage 3. Only 50% of patients who were in stage 4 before the commencement of ART had CD4 count >350 cells/mm^3. The relationship between the WHO clinical stage and the 2 year CD4 count was statistically significant (p= 0.005).

Of the 69 patients who were on cotrimoxazole prophylaxis, 58 (84.4%) were alive and retained in care while 46 (66.7%) had 2 years' post treatment CD4 count of >350 cells/mm^3. On the other hand, 84.4% of the patients who were not on cotrimoxazole prophylaxis were alive and retained in care while 25 (78.1%) had 2 years' CD4 count of >350 cells/mm^3. The relationship between cotrimoxazole prophylaxis and CD4 count is not statistically significant (p= 0.078)

Table 3. *Relationship Between Independent Variables and Patient Outcome.*

	Follow-up status		**CD4 count after 2 years (cells/mm^3)**		
Age (years)	**Retained in care**	**Lost to follow up**	**≤350**	**>350**	**Not done**
<5	6(75.0)	2(25.0)	2(25.0)	6(75.0)	0(0.0)
5-10	59(89.4)	7(10.6)	13(19.7)	50(75.8)	3(4.5)
11-15	20(74.1)	7(25.9)	10(37.0)	15(55.6)	2(7.4)
	x^2 =3.920; df= 2; p=0.141		x^2 =4.215; df= 4 p=0.378		
Sex					
Male	52(85.2)	9(14.8)	18(29.5)	40(65.6)	3(4.9)
Female	33(82.5)	7(17.5)	7(17.5)	31(77.5)	2(5.0)
	x^2 =0.137; df= 1; p=0.712		x^2 =1.986; df= 2; p=0.387		
WHO staging					
1	18(90.0)	2(10.0)	0(0.0)	19(95.0)	1(5.0)
2	38(86.4)	6(13.6)	12(27.3)	30(68.2)	2(4.5)
3	29(82.9)	6(17.1)	13(37.1)	21(60.0)	1(2,9)
4	0(0.0)	2(100.0)	0(0.0)	1(50.0)	1(50.0)
	x^2 =11.342; df= 3; p=0.010		x^2 =18.360; df= 6; p=0.005		
Cotrimoxazole prophylaxis					
Yes	58(84.1)	11(15.9)	21(30.4)	46(66.7)	2(2.0)
No	27(84.4)	5(15.6)	4(12.5)	25(78.1)	3(9.4)
	x^2 =0.002; df= 1; p=0.968		x^2 =5.101; df= 2; p=0.078		

4. Discussion

Introduction of HAART has significantly decreased mortality in HIV-1 infected children. Although an increase in non-HIV related mortality has been noted in adults, data in children are limited. There are limited data regarding causes of death in HIV-1 infected children and changes in such cases over time, most from the pre early HAART era [11-14].

Table 1 highlighted the baseline information of the children. The mean age at presentation was 8.5 years (SD =+ 3.0). Overall, the proportion of males seen in the facility over the review period was higher than the females (60.4% and 39.5% respectively). In our study the outcome of the patients on HAART was quite good; the mortality recorded was 2.0% of the overall patients. This is comparable to what have been observed in the United States and Europe, where there was a temporally reduction in morbidity and mortality with increased use of HAART [11-14]. A likely reason for the low mortality rate in this cohort could be attributed to the fact that most of the children did not have advanced or severe disease at ART initiation as documented in other study [15]. Survival was more among males between 5-10 years and those with WHO clinical stages 1 and 2 disease. Early diagnosis of HIV infection is therefore very important in children in order to initiate them on HAART before they develop advanced or severe disease.

As have been described in smaller cohorts [16-18], we also

found that surviving children generally have very good CD4 cell responses.

5. Conclusion

We found that with availability of ART, the majority of HIV-1 infected children can now be expected to reach adulthood. Challenges for our patients include minimizing toxicity of ART, continued development of ART agents, psychosocial support through adolescence into young adulthood.

Limitation of Study

Despite the defined inclusion and exclusion criteria, some data that would have enriched the quality of the study were missing. These include: the brands of test kits used, the dosage of HAART, brand of medications and how the patients were scheduled for medication and follow up. Furthermore, due to inadequate finances and logistics like epileptic power supply in the country, the number of CD4 tests required for proper monitoring was not adequately captured in the data. However, the baseline and two year CD4 cell count suffice for the aim of the study. Further research will help in developing appropriate care for HIV-infected patients in low income countries like our setting were this study was carried out.

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