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Assessing the Impact of Antiretroviral Therapy on CD4, Hemoglobin Level and Weight in HIV Infected Children (0-15 Years) Residing in Nkambe, North West Region, Cameroon

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Authors' contributions

This work was carried out in collaboration between all authors. Author LEA designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript and managed literature searches. Authors NHN, NAE, CF managed the analyses of the study and literature searches. Author NG did the laboratory work and enter the data. All authors read and approved the final manuscript.

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ABSTRACT

Background: Antiretroviral therapy (ART) has greatly decreased the mortality and morbidity of children living with HIV by reducing the viral load, increase CD4 count thus improving the health of HIV clients. This study seeks to assess the impact of ART on CD4+ Cell Count, weight and haemoglobin level (Hb) in children residing in Nkambe in the North West Region.

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Methodology: A total of 130 HIV infected children within the age range of 5 months to 15years were recruited for the study. Blood samples were collected and used to measure CD4+ and Hb concentrations. Their weights were taken measured using an electronic balance. Hb levels were used to categorized anaemia while growth was assessed using the z scored of weight for age.
Results: Results showed that there was a significant increase (P=0.00) in the mean CD4+, Hb and weight after ART intervention. The prevalence of non-anaemia was higher 52(40.0%) after intervention compared to 30 (23.1%) at the beginning. After initiation, 30 (23.1%), 46(35.4%) and 11(8.5%) children experienced a decrease in their CD4, Hb and weight values, respectively. Of the 30 children with decreased CD4 count, 30(100.0%) were anaemic and 11 (36.7%) were underweight. More females 47(78.3%) experienced increase in $CD4^+$ count while the male children were non anaemic 29(41.4%) and experienced an increase in weight 61(87.1%). Most children of the age group 6-10 years experienced an increase in $CD4^+$ 26(89.7%), Hb 15(51.7%), and weight 25(86.2%) compared to the other age groups.
Conclusion: The use of ART to treat HIV-infected children is effective as it has improved the health of children. In addition this study reinforces the finding that anaemia, low CD4 and poor growth are common among children living with HIV infection.

Keywords: Children; antiretroviral therapy; anaemia; CD4; Hb; weight.

1. INTRODUCTION

The number of children who have human immunodeficiency virus (HIV) continues to increase. Getting an Acquired immunodeficiency syndrome (AIDS)-free generation implies a generation in which all children are born free of HIV and remain so for life or that children living with HIV have access to the treatment [1]. There are about 3.2 million children living with HIV of which 91% reside in sub-Saharan Africa. Of this only 34% of them are estimated to be on antiretroviral therapy (ART) compared to 64% of adults [2]. It has been reported that 90% of the infected infants acquired the HIV from their mothers during pregnancy, delivery, or through breast-feeding [3]. ART has greatly decreased the mortality and morbidity rate in children by 80-90% and 75% respectively such that without treatment, about one third of children living with HIV will die by their first birthday and half die by their second birthday [4]. Thus many children on ART have lived well into adulthood [5-7]. Despite recent efforts to increase access to ART, the scaling up of ART in sub-Saharan Africa faces major challenges which include evaluating CD4 count, viral load and shortage of trained health care personnel [8]. As such WHO now recommend early diagnosis, and immediate treatment of all HIV positive infants and children under the age of five years [9] irrespective of these indicators. Thus this motivated the study to evaluate the effect of ART on children in different areas, cultures and background.

Growth failure, anaemia and decreased immunity are common features of children with HIV infection. The effect of ARTs can be measured at the level of CD4 cell count to determine the immune status; weight to assess growth rate and haemoglobin levels to determine anaemia level. Few studies have evaluated the impact of ART on weight gain, Hb and CD4 counts [7,10]. however this information is still lacking in Cameroon. This study therefore seeks to assess the impact of ART on CD4 Cell Count, weight and Hb levels in HIV positive children on 1 or 2 years first line ART attending an integrated HIV-care clinic. The results of which will be important in the development of the ART guideline in the country.

2. METHODOLOGY

2.1 Study Site

This study was carried out in Nkambe District Hospital which is a rural area with an HIV treatment unit that serves the entire health districts of Nkambe, Nwa and Ako in the Northwest Region of Cameroon.

Ethical Clearance was obtained from the regional delegation of public health and the protocol reviewed by the institutional ethical board. The Parents or guardians of these children as well as the children above 10 years gave their consent after explaining the rational of the study and ensuring their confidentiality.

2.2 Study Population

A total population of 130 HIV infected infants were recruited for the study, 60 males and 70

females within the age range 5 months to 15 years. These children were grouped under the following age stratification; <1 year, 1-5 years, 6-10 years, 11-15 years. The inclusion criteria for the study were as follows: Initiated on ART with at least 1 year of follow-up and having a baseline record of CD4+ cell count, Hb and weight value prior to initiation.

2.3 Sample Collection

Blood samples were collected in blood collection tubes and used to measure CD4+, and Hb concentration. The Hb concentration and the CD4 counts were measured using Urik haematocrit machine and PIMA machine (Alere) following the manufacture's procedure respectively. The weight was taken using an electronic balance (camry). Hb levels were used to categorized anaemia according to age reference standards as follows Non-anaemic ≥11 g/dL, Mild anaemic =10-10.9 g/dL; Moderate anaemia =7-9.9 g/dL and Severe anaemia <7 g/dL [11]. Immunological response was measured by increase in CD4+ from baseline. CD4 count ranges of less than 500 were considered to be low. Improvement in health status or growth was assessed using the z scored for weight and age (WAZ) and classified as severely underweight when Z≤-3; underweight, if Z is between >-3 to -2.1, normal when Z is between -2 to 0 and overweight when Z is > 0 [12]. Data was analyzed using SPSS version 16.0. Independent-Samples T test was used to compare the difference in the means after 1 or 2 years of receiving ART and values at baseline. For categorical variables with more than two categories Chi-Square test was used to determine the association. Pearson's correlation coefficient will be used measure how the variables are related. Significance was considered at $P < 0.05$.

3. RESULTS

3.1 Demographic Information of Participants

In all, 130 children with age range of 0.4 – 15 years with mean (SD) of 7.91(5.2) years were recruited for the study. The highest proportion of children was males 70(53.8%) and the highest number of children 53(40.8%) fell within the age range of 11-15 years (Table 1).

3.2 Effect of ART on $CD4^+$, Hb and Weight

There was a significant increase (P=0.00) when the values of mean CD4+ count, Hb and weight after ART intervention compared to the baseline (Table 2). Evaluating the effect of the duration on ART, only weight had a significant increase (p= 0.00) (Table 3). Based on the type of anaemia, there was an increase in the number of children who were not anaemic at the end of the study period 52 (40.0%). Similarly, fewer children had moderate anaemia 40 (30.8%) at the end compared to what prevailed at the beginning of ART initiation. Equally, more children 114(87.7%) were found to have normal weight at the end of the study (Table 4).

The general trend of the proportion of children who experienced either an increase, a decrease or the same value by the end of the study showed that some children 30 (23.1%), 46(35.4%) and 11(8.5%), had a decrease in their CD4, Hb and weight values respectively while 1(0.8%) and 18(13.8%) children had the same Hb and weight values respectively. Of the 30 children with decrease CD4 count, all the 30 of them (100.0%) were anaemic and 11 (36.7%) were underweight (Table 5). There was a significant correlation between $CD4^+$ and Hb seen one ($r = 0.343$; P=0.00) or two years ($r = 0.590$; P=0.00) after intervention however the correlation was not significant between $CD4^+$ and weight during both intervention (one year: $r = -0.021$; P=0.8 and after two years $r = -0.093$; r=0.29).

Regarding the gender, more female children 47(78.3%) experienced an increase in $CD4^+$ count than their male counterparts. On the contrary more male children were non anaemic 29(41.4%), had an increase in their Hb value 46(65.7%), and experienced an increase in weight 61(87.1) at the end of the study 46(65.7%) compared to their female counterparts (Table 6).

Based on age group, most children of the age group 6-10 years experienced an increase in $CD4^+$ 26(89.7%), were non anaemic 15(51.7), had an increase in their Hb values 23(79.3%), and experienced an increase in weight 25(86.2%) compared to the other age groups. On the other hand most children of the age group < 1 years were found to be anaemic 10(76.9%) and experienced a decrease in weight 3(23.1%) while those of the age group 11-14 years experience a decrease in Hb values 23(43.4%) and were underweight 11(20.8%) Table 7.

4. DISCUSSION

During the study, it was observed that ART had significantly decreased the mortality and morbidity of HIV infected children in the study area. These findings are in conformity with those of other researchers [13,14]. Similar to other studies in resource limited settings, HIV infected children in this study experienced a significant increase in weight, Hb and CD4 after initiation of ART [14,15,10].

Table 1. Demographic characteristics of the study population and base line data

Age group at drug initiation	1 year after ART initiation (%)	2 years after ART initiation (%)	Total (%)
<1 year	0 (0.0)	13 (33.0)	13 (10.0)
1-5 years	18(25.3)	17(28.8)	35(26.9)
6-10 years	20(28.2)	9(15.3)	29(22.3)
11-15 years	33(46.5)	20(33.9)	53(40.8)
Total	**71(54.6)**	**59(45.4)**	**130(100)**
Sex			
Male	40(56.3)	30(50.8)	70(53.8)
Female	31(43.7)	29(49.2)	60(46.2)

Table 2. Effect of ART on $CD4^+$, Hb and weight

Factor (unit)	Intervention phase	Range	Mean (SD)	T value	P value
Weight (kg)	Baseline value	5.00-41.00	20.78(9.92)	-9.49	0.00
	After initiation	6.00-43.00	22.28(9.89)		
$CD4^+$ cells/ mm^3	Baseline value	31-958	468.32(22.42*)	-5.87	0.00
	After initiation	34-1285	670.44(30.6*)		
Hb(g/dl)	Baseline value	7.00-12.30	10.06(1.2)	-5.31	0.00
	After initiation	7.30-14.90	10.94(1.71)		

**Std. error*

Table 3. Effect of duration of treatment on CD4, Hb and weight

Factor (unit)		Years of intervention Mean (SD)		T value	P value
		One year	Two years		
$CD4^+$ cells/ mm^3*	Baseline value	474.71(33.2)	461.90(33.6)	0.32	0.75
	After initiation	654.92(52.1)	639.10(38.9)		
Hb(g/dl)	Baseline value	10.11(1.1)	10.06(1.12)	-0.55	0.59
	After initiation	10.79 (1.8)	10.95(1.5)		
Weight (kg)	Baseline value	22.25 (8.9)	19.06(11.2)	2.1	0.04
	After initiation	23.76 (8.5)	19.71(11.3)		

**Std. Error*

Table 4. Impact of ART anaemia and growth

Factor	Classification	Before ART intervention	After ART initiation	χ^2 value	P value
Anaemia	Non anaemic	30(23.1)	52(40.0)	2.88	0.57
	Mild anaemia	49(37.7)	38(29.2)		
	Moderate anaemia	51(39.2)	40(30.8)		
Growth	Over weight	2(1.5)	2(1.5)	206.4	0.00
	Normal weight	79(60.8)	114(87.7)		
	Underweight	45(34.6)	12(9.2)		
	Severely underweight	4(3.1)	2(1.5)		

Table 5. Impact of ART duration on the proportion of children with increase or decrease $CD4^+$, Hb and weight

Factor	Characteristic (n; %)	Years of intervention n(%)		χ^2 value	P value
		One year	Two years		
$CD4^+$	Decrease value (30; 23.1)	20(28.2)	10(16.9)	2.29	0.10
	Increase value (100; 76.9)	51(71.8)	49(83.1)		
Hb	Decrease value (46; 35.4)	28(39.4)	18(30.5)	2.193	0.33
	Increase value (83; 63.8)	43 (60.6)	40(67.8)		
	The same value (1; 0.8)	0 (0)	1 (1.7)		
Weight	Decrease value (11; 8.5)	7 (9.9)	4(6.8)	15.97	0.00
	Increase value (111; 85.4)	62 (87.3)	49(83.1)		
	The same value (18; 13.8)	2 (2.8)	16(31.1)		

Table 6. Effect of gender and ART on $CD4^+$, Hb and weight

Indicator	Characteristic (n; %)	Female	Male	χ^2	P value
CD4%	Decrease value (30; 23.1)	13(21.7)	17(24.3)	0.13	0.44
cells/µl	Increase value (100; 76.9)	47(78.3)	53(75.7)		
Hb(g/dl)	Non anaemic (52; 40)	23(38.3)	29(41.4)	0.13	0.94
	Mild anaemia (38; 29.2)	18(30.0)	20(28.6)		
	Moderate anaemia(40; 30.8)	19(31.7)	21(30.0)		
	Decrease value (46; 35.4)	23(38.3)	23(32.9)	2.19	0.67
	Increase value (83; 63.8)	37(61.7)	46(65.7)		
	Same value (46; 35.4)	0(0)	1(1.4)		
Weight (kg)	Normal weight(114;87.7)	49(81.7)	65(92.9)	5.84	0.12
	Over weight(2;1.5)	2(3.3)	0(0.0)		
	Severely Underweight (2;1.5)	2(3.3)	0(0.0)		
	Underweight (12;9.2)	7(11.7)	15(7.1)		
	decrease value (46;35.4)	6(10. 0)	5(7.1)	9.30	0.01
	Increase value (101;77.7)	40(66.7)	61(87.1)		
	Same value (18;13.8)	14(22.3)	4(5.7)		

Table 7. Association between age group and ART on CD4, Hb and weight after drug initiation

Indicator	Characteristic (n; %)	Age group in year(s)				χ^2	P value
		<1	1-5	6-10	11-15		
CD4	Decrease value (30; 23.1)	3(23.1)	4(11.4)	3(10.3)	20(10.3)	11.74	0.01
cells/µl	increase value (100; 76.9)	10(76.9)	31(88.6)	26(89.7)	33(62.3)		
Hb(g/dl)	Non anaemic (52; 40)	3(23.1)	16(45.7)	15(51.7)	18(34.6)	13.15	0.04
	Mild anaemia (38; 29.2)	8(61.5)	10(28.6)	8(27.6)	12(22.6)		
	Moderate anaemia(40; 30.8)	2(15.4)	9(25.7)	6(20.7)	23(43.4)		
	Decrease value (46; 35.4)	5(38.3)	12(34.3)	6(20.7)	23(43.4)	6.03	0.42
	Increase value (83; 63.8)	8(61.5)	23(65.7)	23(79.3)	29(54.7)		
	Same value (1; 0.8)	0(0.0)	0(0.0)	0(0.0)	1(1.9)		
Weight	Normal weight (114;87.7)	13(87.7)	33(94.3)	28(96.6)	40(75.5)	23.00	0.01
(kg)	Over weight (2;1.5)	0(0.0)	2(5.7)	0(0.0)	0(0.0)		
	Severely Underweight (2;1.5)	0(0.0)	0(0.0)	0(0.0)	2(3.8)		
	Underweight (12;9.2)	0(0.0)	0(0.0)	1(3.4)	11(20.8)		
	decrease value (11;8.5)	3(23.1)	0(0.0)	1(3.4)	7(13.2)	10.10	0.12
	Increase value (101;77.7)	8(61.5)	30(85.7)	25(86.2)	38(71.7)		
	Same value (18;13.8)	2(15.4)	5(14.3)	3(10.4)	8(15.1)		

The majority of children were males 70(53.8%) and this is in line with other studies carried out by Patel et al. [14], in Surat-India and Kyawswamyint et al. [16] in Myanmar, and contrary to the study carried out in Brazil by Cardoso et al. [6]. USAIDS [3] reported that 90%

of HIV transmission in children is from their mothers during pregnancy, delivery, or through breast-feeding. It is most likely that most male children are breast fed more than female children and as such this accounts for the high prevalence seen in male children. Majority of the children were above 5 years of age which was similar to the findings of Patel et al. [14] and Kyawswamyint et al. [16] but deviates from those of other researchers [17,18]. This supports the fact that without treatment, about one third of children living with HIV die by their first birthday and half die by their second birthday [4]. Although there was an increase in the mean value of $CD4^+$, and Hb observed in children who had received treatment for two years compared to one year, the difference was not statistically significant at p= 0.10 and 0.33 respectively. This suggests that ART yields better outcomes regardless of when it is started. Thus it is possible to use ART to treat HIV-infected children safely and effectively in developing countries with limited resources [19] as in developed countries [20,21].

We recorded a total of 100 (76.9%) children who responded immunological to ART. The high increase in $CD4^+$ cells in the children is similar to those carried out in China [10] and India [14], but lower compared to studies carried out in Dutch [22]. Out of the 30% of children who had <250 cells/µl at baseline CD4, 64.1% of them had the greatest increase in their CD4 at the end of the study period. This was similar to studies carried out in Haiti [23-25]. This supports the fact that the use of ART shows a reduction in viral load and an increase in $CD4^+$ values. The significant $CD4^+$ responses to ART seen in children in the second year of therapy are not in line with those of Ahoua et al. [26] in Uganda and Zheng and Zhao [10] in China, which stated that $CD4^+$ greatly increases in the first than in the second year of therapy. From this study we recorded 26 (20%) children with more than 50% decrease in their $CD4^+$ value. Taking into consideration that we did not look at treatment adherence, we cannot say with certainty that drug failure or resistance can be attributed to the decrease in $CD4^+$. Since these children are mostly orphans and might live in difficult social situations, maintaining good treatment adherence is also challenging. Thus there is need to assess treatment failure as well as drug adherence in this area.

Although a higher proportion of females had a higher CD4 count, on the contrary, increase in weight gain and Hb value was higher in males than their female counterparts. The increase in weight seen in males could be attributed to their eating habits.

As with previous studies [27,28,29] our data suggests that there is a high prevalence of anaemia among children living with HIV infection in Cameroon. This supports the fact that anaemia is recognized as an important clinical problem in HIV-infected patients [15]. The positive effect of ART is probably due to the reduction in viral load, decreased destruction of mature hematopoietic cells and an improvement in erythropoietin response. There was a significant difference seen in the prevalence of anaemia among the age groups ($p< 0.0001$) with the highest prevalence of anaemia (76.9%) seen in children below 1 year. This is possibly due to their increased growth requirements and higher frequency of gastrointestinal infections [30, 31]. The increased prevalence of anaemia in female children 37(61.7%), compared with males 41(58.6%) reflects the overall higher prevalence of anaemia in females, which may be largely attributed to menstrual blood loss as majority of the children 39(65.0%) had reached the age of maturity [32]. Although the prevalence of anaemia decreased, mild-to-moderate anaemia continues to be common. This can also be attributed to inherited haematological disorders, such as sickle cell disease and thalessemia or dietary factors which are common within developing countries. This is in line with the findings of other researchers [33]. Thus the cause of anaemia in HIV-infected children is multifactorial. This is suggestive of the fact that treatment of anaemia should be included in the ART guide line and Hb levels be monitored closely.

This study recorded a significant positive growth correlation ($r = 0.59$) between growth and ART uptake. This was far higher than the 14.8% recorded in Indian children [14]. This is an indication of the benefits of ART with respect to both clinical and immunologic progression of disease [6,7,10]. The 37.7% prevalence of HIV children with underweight was lower compared to the 45% as reported by Yotebieng et al. [8]. Among the 10.7% of children with low weight, 78.6% of them also had a decrease CD4 count. This can probably be attributed to the low T-lymphocyte counts which had been associated with the failure of weight increase [34]. We also recorded 3.1% of children who had normal weight at baseline but later were underweight after drug incitation. This might be attributed to

the presence of other unidentified confounding infections that are exacerbated by acute illness or treatment failure [24]. A significant shift in weight increase from 81 (62.3%) to 116(89.2%) after drug initiation is evidence that ART improves growth in HIV children in addition to the food supplement that are usually given to these children. This is similar to studies carry out in other less develop countries like Haiti [24] and Côte d'Ivoire [20].

5. CONCLUSIONS

This study shows that the use of ART to treat HIV-infected children is effective in resource-limited countries as in developed countries. Better outcomes are achieved regardless of when ART is started. This study reinforces the finding that anaemia, low CD4 and poor growth are common among children living with HIV infection in Cameroon. The data emphasize the importance of initiating ART early to ensure adequate immune and growth responses.

6. RECOMMENDATION

A standard growth curve can be drawn using a larger population size to assess responses to ART to monitor effectiveness of ART in resource-limited settings like ours where it is difficult to get the viral load and CD4 test in monitoring children's responses to ART.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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