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Growth pattern of HIV- infected children on antiretroviral therapy at the Yaounde Gynaeco-Obstetric and Pediatric Hospital, Cameroon

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Abstract

Aim: To assess the growth of HIV-infected children under 15years of age on Antiretroviral therapy (ART).

Methods: We designed a cohort retrospective study at the Yaoundé Gynaeco-Obstetric and Pediatric Hospital (YGOPH) over an 18months period, where files of 85 children aged 6weeks to 15 years were assessed. The Chi-square test was used for the comparison of categorical variables and the Student's t-test for continuous variables. Factors influencing growth were identified by applying multiple logistic regression.

Results: At initiation of treatment, 60% were at least stunted, wasted or underweight (height-for-age Z-score (HAZ) <-2 =51.8%, Weight-for-age Z-score (WAZ)<-2 = 34.6%, Weight-for-height Z-score (WHZ)<-2 =17.8%), after 18months of follow-up, it dropped to 30.6% (21.9% stunted, 14.8% underweight and 7.2% wasted).The mean WAZ increased from -1.36 to -0.63 and mean WHZ increased from -0.27 to 0.18. The mean HAZ change was the least -2.04 to -1.06. Wasting at baseline (aOR= 0.1, CI 95%=0.01–0.88; P= 0.04) was significant for WHZ gain. Stunting at baseline with values (aOR=0.23 CI 95%=0.06–0.86; P= 0.03) and (aOR= 0.12, CI 95%=0.09–0.89; P= 0.019) were significant for WAZ and HAZ gain respectively. Also, parents as main caregiver (aOR= 0.58, CI 95%=0.09–0.81; P= 0.019) were significant for HAZ gain.

Conclusion: Growth of HIV infected children improved on ART and they gained more weight than height during treatment. Adequate nutritional support and early institution of ART are imperative for growth and clinical improvement.

1. Introduction

According to World Health Organization (WHO), human immunodeficiency virus (HIV) continues to be a major global public health issue, having claimed more than 32 million lives so far [1]. There were approximately 37.9 million people living with HIV at the end of 2018, out of which 62% of adults and 52% of children living with HIV were receiving lifelong antiretroviral therapy(ART) and 770 000 people died from HIV-related causes globally [1]. Infection by HIV represents a major pediatric disease worldwide, affecting an estimated of 1.8 million children and adolescents under 15 years of age with an adverse effect on their growth [2]. Complications of HIV in children include; opportunistic infections, growth retardation [3,4], cognitive impairment [3], developmental milestones impairment, pubertal delay [5], chronic skin disease and malignancy [6]. Prior to ART in Africa, studies in HIV-infected children have demonstrated a poor growth outcome marked by high mortality, stunting, and wasting [7].Growth in children is a major health problem in Africa especially in the context of HIV infection, where malnutrition is one of the major complications of HIV/AIDS infection and a significant factor in the progression of the disease [8]. Malnutrition may occur mainly due to; inadequate nutritional intake secondary to anorexia, upper digestive tract lesions and acceleration of protein catabolism [8,9]. Gastrointestinal disorders may result from the HIV infection, opportunistic infections or neoplasms, that damage the mucosa membrane and increases its permeability and will lead to malabsorption of fats, carbohydrates, and proteins, interfering with weight and height development [8–10]. Other mechanisms include: Stress in AIDS, which alters the production of cytokines and promotes

metabolic stress, leading to loss of appetite, anorexia, and catabolism [8,10]. HIV infection can lead to serious growth faltering, although ART initiation will greatly improve it. The aim of our study was to assess the growth trends of HIV-positive children under 15 years of age on ART followed up at the YGOPH

2. Method

2.1 Study setting, sample and data collection

A hospital-based retrospective cohort study design was used. This study was carried out in the pediatric unit of the Yaounde Gynaeco-Obstetric and Pediatric Hospital (YGOPH), from the 8th April 2007 to 25th April 2020 in which we examined the files of HIV infected children aged from 6weeks to 15years who had received treatment for at least 18 months at different intervals (0, 3, 6, 12, 15, 18 months respectively). We excluded, patients started on ART in other health facilities, all patients with incomplete files andchildren with chronic illnesses which can impair growth.Before enrolling each patient, an administrative authorization was obtained from the director of YGOPH to conduct this study in the Pediatric unit and ethical clearance was obtained at the Faculty of Medicine and Biomedical Sciences of Yaounde I. The file numbers of study participants were identified using the enrolment register of all newly diagnosed HIV-infected cases followed up at the hospital. A questionnaire was used to collect the data in which we included; sociodemographic characteristics of the child and main care giver, clinical data (past medical history and anthropometric measurements).

2.2 Statistical analyses

The statistical analyses were performed using SPSS 22.0. Anthropometric data were interpreted using WHO-Anthro version 3.2.2 software and WHO-AnthroPlus version 1.0.4. Values were expressed as mean or median for quantitative variables and frequencies for qualitative variables. Children's growth curves were plotted using the WHO-ANTHRO software. The Chi-square or Fischer test was used for the comparison of categorical variables and the Student's t-test for continuous variables. Factors influencing growth were identified by applying multiple logistic regression. The level of significance was set at $P < 0.05$.

3. Results

3.1 Characteristics of study population

The files of 154 patients were reviewed, out of which 85 files were finally included in our study**.** The data from 69 patients who did not meet the criteria were excluded. There were 47 males and 38 females giving a sex ratio of 1.27. The mean age of the children during study was 9.55±4.19 years and age range of 1.33 to 15years. More than half of the children (57.6%) were in primary school and 30.6% were orphan of either parent or both. The main caregiver was the mother (61.2%). The ages of the caregivers ranged from 25 to 56years with a mean age of 38.24 ±7.49. Most of the parents had a secondary level of education (62.4%) and 8.2% had no formal education, with the majority of them being married (47.1%), 35.3% were single and 12.9% were widow. Most of the caregivers (58.8%) were public servants receiving a monthly salary (Table I).

	Number	Percentage (%)
Age group of children (years) <1	7	8.2
[1 – 5]	14	16.5
[5 – 10]	30	35.3
[10 – 15]	34	40.0
Genderof children		
Male	47	55.3
Female	38	44.7
Level of education of children		
None	11	12.9
Primary	49	57.6
Secondary/higher	21	24.7
University	4	4.8
Main caregiver		
Mother	52	61.2
Father	12	14.2
Relatives	21	24.7
Gender of caregiver		
Female	70	82.4
Male	15	17.6
Age of caregiver		
<25	2	2.4
[25-35]	20	23.5
>35	46	54.1
Unknown	17	20
Level of education of caregiver		
None	7	8.2
Primary	12	14.1
Secondary	53	62.4
High school and above	13	15.3
Occupation of caregiver		
Liberal	50	58.8
Non-liberal	24	28.2
Unknown	11	13
Marital status of caregiver		
Single	30	35.3
Married	40	47.1
Widow	11	12.9
Divorce	3	3.5
Non-documented	1	1.2

Table I: Sociodemographic characteristics of study population

3.2 Mode of transmission, type of diagnostic test, patient characteristics and management at baseline

Mother to child transmission (MTCT) was the main mode of transmission in (89.9%) of these children. Polymerase chain reaction (PCR) base diagnosis was made in 16.5% of HIV-infected children and the majority of these children had HIV type 1 (88.2%) virus and 11.8% had type 1 and 2 viruses. The median age at initiation was 4.0[1.62 – 6.29] years and more than half (51.8%) were diagnosed at a less advance WHO clinical stage (stage 1), 34.1% at stage 2, and 14.1% at a more advanced clinical stage (stage 3 and 4). Only 29.4% received protease inhibitors in their ARV regimen at initiation, Cotrimoxazole was received by the majority of these children (91.8%). The infant feeding method was exclusive breastfeeding in 38.8% and in 40% of the children, the feeding method was unknown.

3.3 Nutritional status and anthropometric variation overtime

Prevalence of malnutrition dropped from 60% at baseline to 30.6% after 18months of follow-up.

Weight-for-height Z-score (WHZ) after ART initiation

The mean WHZ were higher than the other anthropometric parameters at the various follow-up periods. Mean Z-score increased from -0.27 to 0.18 at 18 months after the initiation of ART. The mean WHZ curve increased and reached a peak at 3months, then there's a decrease followed by a plateau from 6 to 9months, then a gradual increase till 18months (Figure 1). Also, the proportion of wasting in children decreased from 17.8% at ART initiation to 7.2% at 18 months after ART. Among the 15 (17.8%) wasted children at baseline, WHZ improved in 9 (60%) patients. The Gaussian curve of our study population at study exit was skewed to the left (proportion with Z score below -2 was 5%) when compared to the WHO reference curve, but was less skewed when compared to the WHZ curve at baseline (proportion with Z score below -2 was 16 %). Children being taken care of by their parents were having 4 more odds (CI 95%=0.08–0.88; P= 0.024) of being wasted during their follow-up. Main caregivers with none and low level of education (primary) were having 4 more odds (CI 95%=0.08–0.88; P=0.032) of their children presenting wasting. Underweight (CI 95%=0.07 – 0.48; P=0.001) and wasting (CI 95%=0.13–0.92; P=0.037) at baseline presented less odds respectively, of being wasted during the follow-up period. After multivariate analysis, being wasting at baseline was retained as a significant factor associated wasted an increase in WHZ at the study exit (Table II).

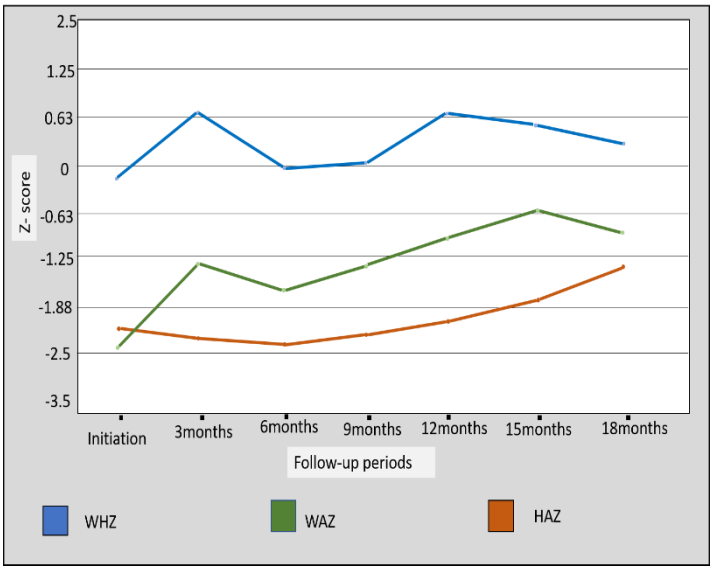

Figure 1: Growth Patterns of HIV-infected children on treatment for 18months following initiation.

Variable		Wasting		OR(CI95%)	P-value	Multivariate Analysis	
		Unfavorable outcome(%)	**Favorable outcome(%)**			**AOR (CI95%)**	**P-value**
Gender	Male Female	23(60.5) 15(39.5)	23(51.1) 22(48.9)	1.48(0.61-3.52)	0.507		
Age at initiation	0 – 59months >60months	24(63.2) 14(36.8)	29(64.4) 16(35.6)	0.95(0.39-2.32)	1.00		
Level of education of child	Not educated Educated	6(15.8) 32(84.2)	5(11.1) 40(55.6)	1.50(0.42-5.37)	0.75	0.28(0.07-1.09)	0.07
Main caregiver	Parents Relatives	33(86.8) 5(13.2)	29(64.4) 16(35.6)	3.64(1.19-11.18)	**0.024**	2.13(0.55-8.19)	0.27
WHO clinical stage	Lessadvanced More advanced	35(92.1) 3(7.9)	36(80) 9(20)	2.92(0.73-11.68)	0.21		
Infant feeding method	Breastmilk Others	13(34.2) 25(65.8)	19(42.2) 26(57.8)	0.71(0.29-1.74)	0.50		
Level of education of caregiver	None and primary Secondary and above	4(10.5) 34(89.5)	14(31.1) 31(68.9)	0.26(0.08-0.88)	**0.032**		
ARV regimen	Protease inhibitors Others	14(36.8) 24(63.2)	11(24.4) 34(75.6)	1.8(0.7-4.65)	0.24		
Wasting at baseline	Yes No	1(2.6) 37(97.4)	14(31.1) 31(68.9)	0.06(0.07-0.48)	**0.001**	0.1(0.01-0.88)	**0.04**

Underweight at baseline	Yes No	8(21.6) 29(78.4)	20(44.4) 25(55.6)	0.35(0.13-0.92)	**0.037**	2.54(0.79-8.15)	0.12
Stunting at baseline	Yes No	20(52.6) 18(47.4)	23(51.1) 22(48.9)	1.06(0.45-2.52)	1.00		
Birth weight	Normal Abnormal	34(89.5) 4(10.5)	36(80) 9(20)	0.47(0.6-2.13)	0.36		

Table II: Factors influencing WHZ change during follow-up

Weight-for-age Z-score(WAZ) after ART initiation

The proportion of underweight children decreased from 34.6% at ART initiation to 14.8% after 18months on treatment. Among the 28 (34.6%) underweight children at baseline, WAZ improved in 16 (57.1%) patients. The mean WAZ-score increased from -1.38 to -0.63 at 18 months after the initiation of ART (figure 1). There was a gradual increase of the mean WAZ curve from baseline with little fluctuation between 15 and 18months. At study exit, the Gaussian curve was less skewed to the left when compared to the curve of our study population at initiation with respect to the WHO reference curve. Children presenting underweight (OR= 0.06;CI 95%=0.01-0.44;P=0.00) and stunting(OR= 0.11;CI 95%=0.03-0.37;P=0.00) at baseline had less odds of being underweight during the follow-up period(table III). After multivariate analysis, stunting at baseline was retained as a significant factor associated with increase in WAZ at the study exit (Table III).

Variable		**Underweight**		**OR(CI95%)**	**P-value**	**Multivariateanalysis**	
		Unfavorableoutcome (%)	Favorable outcome(%)			AOR(CI95%)	P-value
Gender	Male Female	12(52.2) 11(47.8)	31(53.4) 27(46.6)	0.95(0.36–2.5)	1.00		
Age at initiation	0 – 59months >60months	14(60.9) 9(39.1)	40(69) 18(31)	1.43(0.52–3.9)	0.60		
Level of education of child	Not educated educated	4(17.4) 19(82.6)	7(12.1) 51(87.9)	1.53(0.4 – 5.84)	0.50		
Gender of caregiver	Male Female	2(8.7) 21(91.3)	12(20.7) 46(79.3)	0.37(0.08-1.78)	0.33		
Main caregiver	Parents Relatives	15(65.2) 8(34.8)	45(77.6) 13(22.4)	0.54(0.19–1.6)	0.27		
WHO clinical stage	Less advanced More advanced	20(87) 3(13)	49(84.5) 9(15.5)	1.22(0.3– 5.0)	1.00		
Infant feedingmethod	Breastmilk Others	6(26.1) 17(73.9)	26(44.8) 32(55.2)	0.44(0.15-1.26)	0.14		
Level of education of caregiver	None and primary Secondary and above	3(13) 20(87)	15(25.9) 43(74.1)	0.43(0.11-1.66)	0.25		
ARV regimen	Protease inhibitors Others	7(30.4) 16(69.6)	18(31) 40(69)	0.97(0.34–2.7)	1.00		

Wasting at baseline	Yes No	3(13) 20(87)	12(20.7) 46(79.3)	0.58(0.15-2.26)	0.54		
Underweight at baseline	Yes No	1(4.3) 22(95.7)	26(44.8) 32(55.2)	0.06(0.01-0.44)	0.00	7.52(0.79-8.15)	0.07
Stunting at baseline	Yes No	4(17.4) 19(82.6)	38(65.5) 20(34.5)	0.11(0.03-0.37)	0.00	0.23(0.06-0.86)	0.03
Birth weight	Normal Abnormal	18(78.3) 5(21.7)	51(87.9) 7(12.1)	0.61(0.07–5.8)	1.00		

Table III: Factors influencing WAZ change during follow-up

Height-for-age Z-score (HAZ) after ART initiation

HAZ had the least increase during the ART period. Mean Z-score increased from -2.04 to -1.06 at 18 months after the initiation of ART.The mean HAZ decreased slightly from baseline, and at six months there was a gradual and stable increase of this parameter till the end of follow-up. Correspondingly, the proportion of stunted children decreased from 51.8% at ART initiation to 21.9% at 18 months after ART. Among the 44 (51.8%) stunted children at baseline, HAZ improved in 26 (21.9%) patients. The Gaussian curve of our study population at study exit was skewed to the left (proportion of children with Z score below -2 was 17%) when compared to the WHO reference curve, but it was less skewed when compared to the HAZ curve at baseline (proportion of children with Z score below -2 was 20%). Children being taken care of by their parents (OR= 0.28;CI 95%=0.1 – 0.83;P=0.04)and who were having stunting at baseline(OR= 0.26;CI 95%=0.09–0.77;P=0.02), were having less odds of being stunting (Table IV). After multivariate analysis, children with stunting at baseline and who were being taking care of by their parents were retained as significant factors associated with increase in HAZ at study exit (Table IV).

Variable		**Stunting**		**OR(CI95%)**	**P-value**	**Multivariateanalysis**	
		Unfavorableoutcome(%)	Favorable outcome(%)			AOR(CI95%)	P-value
Gender	Male Female	12(57.1) 9(42.9)	35(55.6) 28(44.8)	1.07(0.39–2.89)	1.00		
Age at initiation	0-59months >60months	40(63.5) 23(36.5)	14(66.7) 7(33.3)	0.87(0.31–2.47)	0.13		
Level of education	Not educated Educated	5(23.8) 16(76.2)	6(9.5) 57(90.5)	2.97(0.8–11.00)	0.13		
Gender of caregiver	Male Female	4(19) 17(81)	10(15.9) 53(84.1)	0.80(0.35–4.49)	0.74		
Main caregiver	Parents Relatives	12(57.1) 9(42.9)	52(82.5) 11(17.5)	0.28(0.1 – 0.83)	0.04	0.58(0.09-0.89)	0.031
WHO clinical stage	Lessadvanced More advanced	16(76.2) 5(23.8)	56(88.9) 7(11.1)	0.4(0.11-1.43)	0.16		
Infant feedingmethod	Breastmilk Others	7(33.3) 14(66.7)	26(41.3) 37(58.7)	0.71(0.25-2.01)	0.61		
Level of education of caregiver	None and primary Secondary and above	4(19) 17(81)	15(23.8) 48(76.2)	0.75(0.22-2.59)	0.77		
ARV regimen	Protease inhibitors Others	7(33.3) 14(66.7)	18(28.6) 45(71.4)	1.25(0.43-3.61)	0.78		
Wasting at	Yes No	6(28.6) 15(71.4)	9(14.3) 54(85.7)	2.4(0.74-7.82)	0.19		

baseline							
Underweight at baseline	Yes No	5(23.8) 16(76.2)	23(37.1) 39(62.9)	0.53(0.17-1.64)	0.30		
Stunting at baseline	Yes No	6(28.6) 15(71.4)	38(60.3) 25(39.7)	0.26(0.09-0.77)	0.02	0.12(0.09-0.81)	0.019
Birth weight	Abnormal Normal	5(23.8) 16(76.2)	8(12.7) 55(87.3)	1.37(1.2-1.57)	0.30		

Table IV: Factors influencing HAZ change during follow-up

4. Discussion

This study describes the growth trend of HIV infected children aged between 6weeks to 15years after initiation of ART.We found that weight-for-height Z-score, weight-for-age Z-score and height-for-age Z-score improved after the initiation of ART, just like previous studies in other countries. The overall prevalence of malnutrition at baseline (initiation) was 60%. This prevalence was in line with result obtained by Anyabolu et al (58.6%) in Nigeria [11], less than that found by Chiabi et al.(66.7%) in Yaoundé [4], and Penda et al.(68.7%) in Douala [12]. These differences can be explained by the varying prevalence of malnutrition among HIV-infected children in different countries, early initiation of ARV before the onset of severe clinical signs of immunosuppression and by the different sample sizes in different studies.

Weight for Height Z scores (WHZ) less than -2 reflect acute malnutrition (wasting). The prevalence of wasting was 17.8% at baseline. This was lower than that of Chiabi et al.(41.4%) [4]. This higher prevalence could be due to the fact that they were prospective studies and the prevalence of wasting was measured over a period of 12 months, whereas we measured our proportion only at initiation of ART. Our prevalence was greater than 9.7% found by Raghavendra et al in India [13]. This could be explained by the low mean age of ARV initiation of our study (4years) compared to 11years of Raghavendra et al, since the immune system is not yet fully matured and severe stages of immunosuppression can easily be reached. The mean WHZ were higher than the other anthropometric parameters at the various follow-up periods with many fluctuations. These fluctuations could probably be explained by anorexia and diarrhoea which occurs commonly in HIV-infected children resulting in acute weight loss. The drop in proportion of children with Z score (below -2) out of the Gaussian curve from 16%(at initiation) to 5%(study exit) was due to the chronic suppression of the viral load by ART thereby reducing the vulnerability to infections, decreasing the production of cytokines and metabolic stress which reduces catabolism [8], hence improvement of nutritional status. Wasting at baseline was retained as a significant factor associated with an increase in WHZ at the study exit. Children who were wasted at initiation of ARV were given nutritional support. This could account for the improvement in their Z scores as shown by some studies [7,13].

The weight for age Z-scores (WAZ) less than -2 indicates underweight. Children who had WAZ< -2 were 28(34.6%). In the 2018 demographic health survey, the prevalence of underweight in Cameroon was 4% which is lower than what we observed in our study [14]. In Cameroon, Chiabi et al, and Penda et al showed a much higher prevalence of underweight in their studies (56.4%, and 37.8% respectively) [4,12] and similar findings were reported by other studies in and out of Africa [11,15,16]. The lower proportion of under-nutrition in our study as compared to other studies may be explained by the fact that most of these studies had higher sample sizes.

During treatment there was a gradual increase of the mean WAZ from baseline right up to three months, then there was a decrease without reaching the lowest point (base line) followed by a stable and gradual increase with little fluctuation between 15 and 18months. Hu et al. in China also observed a stable increase in WAZ after initiation of ART. Similar studies have described weight gain towards normal levels [4,13,17]. Kabue et al. reported a gain in the WAZ but it did not reach the normal levels, and these findings were consistent in some other studies [7].In a study by Nachman et al. in the USA, they observed that ART improved the weight gain of children from growth retardation to normal growth after one year of treatment, and this was because the mean WAZ at ART initiation of their study (-0.16) was much lower than that in our study [18]. Stunting at baseline was retained as a significant factor associated with increase in WAZ at the study exit. This could be explained by the fact that more emphasis was placed on children presenting malnutrition at initiation by providing nutritional support [17].

Height for age Z scores (HAZ) less than -2 indicates stunting. Stunting was the most common form of growth retardation with a prevalence of 51.8%. This finding was in line with that of Chiabi et al. in Cameroon who had 51.3%, and lower than Sofeu et al. with a prevalence of 60.4%, 63.6% by Penda et al. and several other studies had a higher prevalence too [15,16,19]. This could be because most of these studies had higher sample sizes than ours and thus a better representation. The HAZ score change was the least, and it changed from -2.04 to -1.06. Most studies also observed that majority of these children did not reach their normal heights over time and in our study stunting was still a problem at study exit in 18 (21.9%) of children [12,20]. This could be because stunting is a chronic process and since the median age of ART initiation was late, it indicates a longer duration of infection thus chronic effect on height. In a study in the USA, they observed that ART improved the HAZ and height was gained to normal after two years on ART [18]. This could be explained by the fact that their baseline HAZ was much higher (-0.57) than that observed in our study. After multivariate analysis, stunting at baseline was retained as a significant factor associated with increase in HAZ at the study exit. This could be explained by the fact that more emphasis was

placed on children presenting malnutrition at initiation by providing nutritional support, which greatly improves nutritional status [17].

5. Conclusion

The growth of HIV infected children improved on ART and these children gained more weight than height during treatment. It will thus be important to integrate anthropometric parameter monitoring during follow-up of HIV infected children. Additionally, adequate nutritional support and early institution of ART in HIV infected children are imperative for growth and clinical improvement. The main limitation of the study was the fact that it was a retrospective study and the data were taken from the files and not by the authors. This might have led to some bias in the measurement.

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List of abbreviations:

WHO: World Health Organization
HIV: Human Immuno deficiency syndrome
ART: Anti retroviral therapy

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