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Research Article

Prevalence of Pubertal Delay in Paediatric Human Immunodeficiency Virus Infection

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Abstract

Background: In Cameroon, Paediatric HIV occurs in 7 per 500,000 people living with HIV. HIV infection can result in impaired sexual development and delayed puberty. There are few studies on the impact of HIV on puberty.

Aim: To determine prevalence of pubertal delay in paediatric population infected with Human Immunodeficiency Virus (HIV) on antiretroviral therapy.

Methods: This was a cross-sectional descriptive study that assessed puberty using the Marshall and Tanner staging system in 120 HIV positive children aged 8-18years, at the Bamenda Regional Hospital treatment Centre from February to May 2022. Data obtained included sex, age, tanner stage of development and age at puberty.

Results: Of 120 participants included, the majority 64(53.3%) were girls. The median (IQR) age was 13.9(11.1-15.8) and 71(59.2%) were aged ≥13years. Sixty-three (52.5%) participants were in Tanner stage 1-2 and the prevalence of pubertal delay was 12.7%. Median age at puberty in years was thelarche: 12.5(9.9-14.4), adrenarche: 13.2(11.8-14.6), menarche: 14(13-14) in girls and gonadarche: 12.9(11.6-14.4), adrenarche: 13.3(11.4-14.4) in boys.

Conclusion: About 13% of HIV infected children on ART experience pubertal delay with a prevalence rate of 12.7%.

Keywords: Puberty; Human immunodeficiency virus; Paediatrics

Introduction

Human Immunodeficiency Virus (HIV) in the paediatric population contributes to the high burden of infection in children aged 1-14 years and accounts for 1.7 million cases and 150,000 new infections annually with the Sub-Saharan Africa most affected [1]. In Cameroon, paediatric HIV occurs in 7 percent of 500,000 people who are living with HIV [2]. Morbidity and mortality from thisinfection is high and results in multi-systemic involvement including the endocrine system. Onset of puberty heralds sexual development and is enhanced by sex hormones bringing about body changes and self-image. HIV infection results in impaired physical growth, wasting and resultant hypofunction of hypothalamic-pituitary gonadal axis resulting in impaired sexual development and delayed puberty [3-11]. Delayed puberty refers to lack of features of pubertal development by the age of 13 years in females and 14 years in males [13,14]. There are few studies on impact HIV on puberty and in Cameroon there is limited data on puberty in the paediatric HIV population, hence the necessity of this study to determine the prevalence of pubertal delay in a paediatric HIV infected population on Antiretroviral Therapy (ART) at a treatment centre in Cameroon.

Methods

Study Design and Setting

This was a hospital-based cross-sectional descriptive study over a 4 months period, carried out in the paediatric treatment centre of the Bamenda Regional Hospital (BRH); a second-level reference health institution for the North West Region of Cameroon. This facility follows up over 500 children aged between 0-19 years living with HIV and receiving Antiretroviral Therapy (ART) of which 250 are aged 8-18 years.

Study Population

Children aged 8-18 years who were HIV infected and followed up at the paediatric treatment centre of BRH whose parent or guardian consented to the study and who gave assent to participate in the study were included while those with chronic illnesses or genetic abnormalities such as sickle cell disease, congenital heart disease, chronic renal failure, diabetes, inflammatory bowel diseases, paediatric malignancies, genetic diseases (Downs syndrome, Turners syndrome) were excluded.

Ethical Consideration

Ethical clearance was obtained from the Institutional Review Board of the Faculty of Health Sciences, University of Bamenda and administrative authorization was also gotten from the North West Regional delegation for public health and the Bamenda Regional Hospital. Informed consent from the caregivers and assent from the children.

Study Procedure

Data Collection

Socio-demographic data was obtained in a structured preformed questionnaire and records of the physical examination to demonstrate features of sexual maturity. Sexual maturation was assessed by

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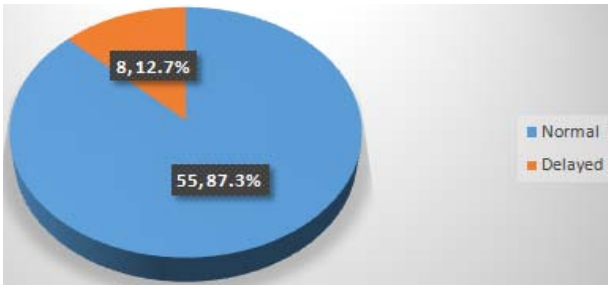

Figure 1: Prevalence of pubertal delay in study population.

physical examination with the aid of graphic representations of the Marshall and Tanner staging system. This staging system grades pubertal development via assessment of external primary and secondary sexual characteristics in the subjects on a 5point ordinal scale in both boys and girls that ranges from 1 (pre pubertal) to 5 (adult like) for female breast, male genitalia and pubic hair for both males and females. Female participants were asked about their age at attainment of menarche.

Data Analysis and Management

Data obtained was entered into the software statistical package for social sciences (SPSS) version 26.0 for analysis. Quantitative variables were expressed as mean ± SD for normal distribution and medians and Interquartile Range (IQR) for non-normal or skewed distribution. Categorical variables were expressed as frequency and percentages.

Results

General Characteristics of Study Participants

Table I highlights the socio-demographics of the 120 enrolled participants consisting of 64 (53.3%) female and 56 (46.7%) male with a female to male ratio of 1.1.Most of the subjects were above 13 years

Table 1: Sociodemographic profile of participants and guardians (N=120).

Variable		Frequency(n)	Percentage(%)
Age groups			
	8 to <10 years	15	12.5
	10 to <13 years	34	28.3
	≥13 years	71	59.2
Median(IQR) age	13.9(11.1-15.8)		
Gender			
	Male	56	46.7
	Female	64	53.3
Age distribution in males(N=56)			
	8 to <10 years	5	8.9
	10 to <14 years	26	46.4
	≥14 years	25	44.6
Age distribution in females(N=64)			
	8 to <10 years	10	15.6
	10 to <13 years	16	29.7
	≥13 years	38	54.7

IQR interquartile range

Table 2: Tanner stages by age group in boys and girls (N=120).

Tanner stage		Age groups n(%)			Delayed n(%)
		8 to<10 years	10 to <13 years*/ 10 to <14 years**	≥13 years*/ ≥14 years**	
Breast development (N=64)					
	B 1-2	10(37.0)	14(51.9)	3(11.1)	3(4.7)
	B 3-5	0(0)	2(5.4)	35(94.6)	
Genitalia development (N=56)					
	G 1-2	5(13.9)	26(72.2)	5(13.9)	5(8.9)
	G 3-5	0(0)	0(0)	20(100)	

* for breast development, **for genitalia development

Table 3: Median Age at Tanner stages and menarche in girls (N=120).

Tanner stage	Frequency (percentage)	Age median (IQR)/years
GIRLS (N=64)		
Breast development (B)		
B1	22(34.4%)	10.5(9.1-11.4)
B2	5(7.8%)	12.5(9.9-14.4)
B3	11(17.2%)	14.3(13.2-15.2)
B4	12(18.7%)	15.3(14.8-15.8)
B5	14(21.9%)	17.2(16.2-17.7)
Pubic hair development (PH)		
PH 1	23(35.9%)	10.5(9.0-11.3)
PH 2	4(6,3%)	13.2(11.8-14.6)
PH 3	10(15.6%)	14.2(12.9-15.7)
PH 4	14(21.9%)	15.2(14.9-15.9)
PH 5	13(20.3%)	17.2(16.5-17.7)
Menarche	31(49.2%)	14.0(13.0-14.0)
BOYS (N=56)		
Genitalia development (G)		
G1	24(42.9)	11.2(10.1-13.2)
G2	12(21.4)	12.9(11.6-14.4)
G3	3(5.4)	15.9(14.9-15.8)
G4	10(17.9)	15.6(15.5-16.7)
G5	7(12.5)	17.3(16.3-17.5)
Pubic hair development (PH)		
PH 1	25(44.6)	11.2(10.1-13.2)
PH 2	11(19.6)	13.3(11.4-14.7)
PH 3	2(3.7)	15.7(14.9-15.7)
PH 4	11(19.6)	15.6(15.5-16.7)
PH 5	7(12.5)	17.2(16.3-17.5)

IQR interquartile range

(59.2%) followed by those aged [10-13] years constituting 28.3% while those aged 8 to less than 10 years were the minority.

Tanner Staging in Males and Females

Table II represents puberty in females and males by age groups using breast and genitalia development respectively. Three out of 27 (11.1%) girls were in Tanner stage 1-2 for breast development in those aged 13 years or older while five out of thirty-six (19.9%) boys aged

14 years or older were in Tanner stage 1-2 of genitalia development. Amongst those with advanced puberty, very few females 2(5.4%) were aged between 10 and 13years and there were no males aged 10-14 years in advanced stages of puberty.

In table III, the median (IQR) age in years at Tanner stage 2 for breast and pubic hair development was 12.5 (IQR 9.9-14.4) and 13.2 (IQR 11.8-14.6) in girls. More than half of the girls 33(50.8%) had not attained menarche. The median (IQR) age at menarche was 14.0(13.0-14.0) years. The median (IQR) age in years at Tanner stage 2 of genitalia and pubic hair development were 12.9(11.6-14.4) and 13.3(11.4-14.7) years respectively in boys.

Pubertal Delay

Pubertal delay was defined as the presence of Tanner stage 1 or Tanner stage 2 at an age ≥ 2SD from the expected mean for Tanner stage 2 breast and genitalia development, which is 13years in females and 14years in males [7,8]. Using these cut-off ages, sixty-three participants, who accounted for 52.5% of the study population were assessed for delayed puberty. The overall prevalence of pubertal delay was 12.7% (95% CI: 4.5-20.9) as shown in figure 1. The prevalence in girls was 7.9% (3/38) and 20% (5/25) in males.

Discussion

The prevalence of pubertal delay in our study population was 12.7%; with majority of boys (20%) experiencing delayed puberty compared to 7.5% in girls. Our results are higher than the 8.7% and 4.1% reported by Nana and collaborators in Uganda and Williams *et al* in the USA respectively [9,10]. Nana and colleagues only included patients on PI-boosted second line antiretroviral therapy [10] while Williams and colleagues studied a mixed racial population in a country with high living standards and consequently better nutrition and growth; different from our study involving subjects on other non PI based regimens and a cluster of purely black race in a developing country in a region plagued with war, poverty and food scarcity. Contrarily, McHugh *et al* found an even higher prevalence of 21% in HIV infected adolescents in Zimbabwe [11]. They had gender specific prevalence of 27 per 100 in girls and 13 per 100 in boys [11,12]. This higher prevalence could be because their participants had no prior antiretroviral therapy, whereas, in our study, all participants were already on ART for an average duration of 8years buttressing the benefits of antiretroviral therapy in infected children. Pubertal delay was more common in boys in our study which could be because of the usual earlier onset of puberty in girls regardless of their HIV serological status. The prevalence of pubertal delay in our study population amongst girls was comparable to the prevalence of 6.25% obtained in Nigeria by Iloh *et al*, [3] which could be explained by similarity in methodology. However Mbono et al in Yaounde, in Cameroon; among a similar population did not observe delay pubertal delay [13] despite similarities in study method.

The age of attainment of puberty in Cameroon among normal non-HIV infected children was reported at 8.9 years for girls and 9.6 years for boys [14]; which is earlier than the 12.5 years and 12.9 years respectively noted in our study population. (highlighting the impact of the disease on puberty). The age at onset of puberty in girls and boys in our study was similar to those of other authors in Africa and Europe [3,5,6] but different from Mbono et al and Buchacz et who found an earlier age at puberty [4,13]. Our observations may be due to the fact that majority of our subjects were in advanced stage of the disease at the time of diagnosis which may have been associated with an increase in the viral load and further depletion of immune function, increasing susceptibility to infections and increasing inflammatory markers; hence negatively affecting nutrition via decreased intake and poor absorption leading to impaired growth and resultant impairment of pubertal development via leptin hypo-secretion [16-18] as seen with most chronic diseases [16,19,20].

Conclusion

The age at onset of puberty in the paediatric HIV population on ART in our study was 12.5 years in females and 12.9years in males with the prevalence of pubertal delay of 12.7% which was high. More males than females experienced delayed puberty.

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