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A Comparative Study of Pubertal Development in HIV-Infected and Non-HIV-Infected Boys in Port Harcourt, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Pubertal abnormalities can occur in HIV-infected boys and have negative effects on reproductive health, final adult height as well as psychosocial health and quality of life. This study was aimed at comparing the pubertal development in HIV-infected and non-HIV-infected boys attending two tertiary hospitals in Port Harcourt.
Materials and Methods: A Comparative cross sectional study was carried out involving 80 HIV-infected boys aged 10-18 years and 80 non-HIV-infected boy who were matched for age, sex and socioeconomic class.
Results: The mean age of the HIV-infected boys was 13.22±2.31 while that of the non-HIV-infected boys was 13.24±2.30 and this difference was not statistically significant. On physical evaluation using the Tanner staging method, only 64 (80%) HIV-infected boys had attained puberty as against 76 (95%) in the non-HIV-infected group (χ^2= 13.091, p-value=0.011). Pubertal onset

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occurred at a significantly later age in HIV-infected boys when compared to the non-HIV-infected ones (11.76±1.33 years vs 10.81±0.77 years). Pubertal delay was seen in 2 (2.5%) and this was significantly more common among those who were underweight as well as those in WHO clinical stages 3 and 4.

Conclusion: Pubertal onset occurred at a significantly later age in HIV-infected boys when compared to the non-HIV-infected boys. There is need to monitor pubertal development in HIV-infected boys so that deviations from normal can be promptly identified and necessary interventions given.

Keywords: Puberty; HIV-infected-boys; Port Harcourt.

1. INTRODUCTION

Puberty is a complex developmental process which begins in late childhood and is triggered by maturation of the hypothalamic-pituitary-gonadal axis [1]. Pulsatile activity of the neuronal network of the gonadotropin releasing hormone leads to a surge in gonadotropin secretion leading to the appearance of secondary sexual characteristics, growth spurt and ultimately the capacity for fertility and reproduction [2-4].

The commonest clinical system for describing normal pubertal development and its variation is the five-stage system developed by Tanner in [5]. In boys, the onset of puberty is marked by testicular enlargement followed by the appearance of pubic hair, enlargement of the penis and first seminal emission (spermarche) [5].

Disorders of pubertal development may occur at any stage of the maturational process leading to either precocious or delayed puberty [4]. Pubertal development is influenced by genetic factors, nutrition, environmental factors and chronic diseases [1,6].

Human Immunodeficiency Virus (HIV) / Acquired Immunodeficiency Syndrome (AIDS) and the attendant chronic immunosuppression have been shown to affect the pubertal development of children [7-10]. In HIV-infected children, pubertal delay which is defined as the absence of secondary sexual characteristics at an age ≥2 standard deviation above the mean for age and sex is the most common pubertal abnormality seen [11,12]. In boys, puberty is considered delayed if testicular enlargement does not occur by 14 years of age, there is lack of pubic hair by 15 years or more than 5 years are required to complete genital development [1,13].

The mechanisms of pubertal delay in HIV-infected children are largely unknown. However, mechanisms postulated include nutritional deficiencies, recurrent infections and chronic immune activation which may all distort the endocrine axes [8].

Similarly, precocious puberty has also been reported in HIV-infected boys [11]. This is defined as the appearance of secondary sexual characteristics before the age of nine years in boys [11].

With a large number of HIV-infected children now surviving into adolescence as a result of advancements in the management of HIV and AIDS, pubertal developmental disorders may pose an increasing challenge [14].

Unidentified pubertal disorder may be associated with risk for psychosocial problems including low self-esteem and depression and may also have negative implications for reproductive health and final adult height [10,15-16]. This thus underscores the need to study pubertal development in HIV-infected children.

When identified early, adolescents with pubertal delay can benefit from interventions such as psychological support, nutritional support and possibly low dose of gonadal steroid hormones or growth hormone in addition to Highly Active Antiretroviral therapy (HAART) [8,9,17,18]. Similarly, HIV-infected children with precocious puberty may benefit from psychological support in addition to HAART to help limit the impact of chronic immunosuppression on the endocrine axis. In some cases, gonadotropin releasing hormone agonists such as leuprolide may help restore final adult height [8,19]

This study was aimed at evaluating the pattern of pubertal development among HIV-infected boys in comparison to non-HIV-infected boys in Port Harcourt, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Design

A comparative cross sectional study design was used. The study was carried out over a four month period (July 1st –October 31st 2017).

2.2 Study Area

The study location was the Paediatric departments of the University of Port Harcourt Teaching Hospital (UPTH) and the Rivers State University Teaching Hospital (RSUTH). The two hospitals are both tertiary care facilities located in the city of Port Harcourt and providing Antiretroviral (ARV) care for HIV-infected.

2.3 Study Population

This study involved 80 boys age 10-18 years with confirmed HIV infection and on follow up at the Paediatric ARV clinic. Similarly, 80 non-HIV-infected boys were recruited from the children's outpatient clinic and matched for age, sex and socioeconomic class to serve as a comparison group. HIV-infected boys who had other chronic disease conditions like sickle cell anaemia which can also affect pubertal development were excluded from the study.

2.4 Study Procedure

HIV-infected boys receiving follow up care at the paediatric ARV clinic were consecutively recruited over a four month period. For each HIV-infected subject, a comparison matched for age, sex and socioeconomic class was recruited. HIV infection was excluded through rapid diagnostic testing before enrolment of the comparison group. History and physical examination were used to exclude the presence of other chronic diseases that can affect pubertal development such as chronic kidney diseases and bronchial asthma.

Relevant sociodemographic data and information on age of attainment of pubertal indices were obtained using a semi-structured interviewer administered questionnaire. This was followed by physical examination of the boys to determine the pubertal stage status using the Tanner staging system for testicular and pubic hair development. Testicular volume was determined using an Orchidometer.

2.5 Statistical Analysis

Data analysis was done using SPSS version 20.0. Results were presented as tables and charts in simple proportions. Student t-test was used for the comparison of means while Chi square and Fisher exact test was used to test for associations between categorical variables. Statistical significance was at 95% confidence interval with p-value<0.05.

3. RESULTS

The study participants consisted of 80 HIV-infected boys and 80 non-HIV-infected boys. The mean age of HIV-infected boys was 13.33±2.42 years while that of non-HIV-infected boys was 13.34±2.43 years (t=0.0261, p=0.9792).

Using both recall of pubertal events and physical examination method (Tanner staging), pubertal onset occurred at significantly later ages in HIV-infected boys compared to the non-HIV-infected ones (Tables 1 and 2). Other pubertal events such as pubic hair development, axillary hair development and spermarche also occurred at significantly later ages in the HIV-infected group (Table 1).

Table 3 shows that a lower proportion of HIV-infected boys had attained puberty (Tanner stage 2 and above for genital development) in comparison to the non-HIV-infected boys (χ^2=13.091,p-value=0.011). There was however no significant difference between the two groups in terms of the final pubertal outcome (Table 4).

4. DISCUSSION

Our study found the mean age of pubertal development in HIV-infected boys using both the recall and physical examination of Tanner stages to be significantly higher in comparison to non-HIV-infected boys. This is understandable as HIV infection and the attendant immunosuppression is known to exert a negative effect on the pubertal development process. Similar findings have also been reported in some previous studies [9,20,21].

The mean age of pubertal onset in HIV-infected boys in the index study was 11.76 years. This compares favorably with that reported by Buchacz *et al*, [9] and Williams *et al*, [20] both in the USA. It is however lower than the 13.5 years reported by Mbwile, [7] in Tanzania and 12.8

years reported by Szubert *et al*, [8] in Uganda and Zimbabwe. Other factors influencing pubertal development such as nutrition and environmental exposures may have contributed to the variations in the mean age of pubertal onset among the various studies in comparison.

The mean age of completion of pubertal development as evidenced by attainment of Tanner stage 5 for genital and pubic hair development was higher in HIV-infected boys compared to non-HIV-infected ones. This difference was however not statistically significant. A significantly lower proportion of HIV-infected boys than non-HIV-infected ones were found in the more advanced pubertal stages (Tanner stages 3-5). Similar findings were reported in previous studies [9,22]. This may be explained by the deleterious effects of HIV infection on the hypothalamic-pituitary-gonadal axis leading to delays in progression through the pubertal stages.

With regard to pubertal stage status, majority of the children studied had normal pubertal stage status. Pubertal delay was however found in 5% of the HIV-infected boys and none in the non-HIV-infected. The higher prevalence of pubertal delay seen in HIV-infected boys is similar to that reported by Shadab *et al*, [23] in India. The proportion of HIV-infected boys with pubertal delay in our study also compares favorably with that reported in the Indian study. In contrast, Mbono et al, [24] reported normal pubertal development among all the HIV-infected boys evaluated in a study done in Cameroun.

One HIV-infected child reported precocious puberty in the index study. This is an uncommon finding and the explanation for this is unknown. However, Horner and Bhumbra, [11] have also reported a case of precocious puberty diagnosed in a perinataly HIV-infected boy in the USA. It would be important to exclude other underlying causes of precocious puberty in such children.

Table 1. Comparison of mean age at onset of pubertal events (by recall) in male study subjects

	Males			
Pubertal event recall	**HIV-infected Mean age ± S.D (years)**	**Non HIV-infected Mean age ± S.D (years)**	**t**	**p-value**
Genitals	12.04 ± 1.05	11.46 ± 0.88	2.943	0.004*
Pubic hair	12.04 ± 1.04	11.40 ± 1.25	2.767	0.007*
Axillary hair	12.42 ± 1.08	11.89 ± 0.90	2.403	0.019*
Spermarche	14.80 ± 0.41	13.86 ±0.71	5.162	0.0001*

**Statistically significant, S.D-Standard Deviation*

Table 2. Comparison of mean ages of male study subjects at various tanner stages

	Males			
Tanner stages	**HIV-infected Mean age ± S.D (years)**	**Non HIV-infected Mean age ± S.D (years)**	**t**	**p-value**
Genitals				
G1	11.46 ± 1.61	10.80 ± 1.02	0.769	0.452
G2	11.76 ± 1.33	10.81 ± 0.77	2.558	0.015*
G3	13.14 ± 2.04	12.73 ± 1.72	0.699	0.489
G4	15.14 ± 1.72	14.13 ± 1.71	1.679	0.103
G5	16.94 ± 0.68	16.30 ± 1.45	1.318	0.199
Pubic hair				
PH1	11.66 ± 1.50	10.59 ± 0.63	1.799	0.086
PH2	11.87 ± 1.63	11.40 ± 1.28	1.057	0.296
PH3	13.50 ± 2.00	12.87 ± 2.03	0.782	0.442
PH4	14.04 ± 1.79	13.38 ± 0.66	1.155	0.262
PH5	16.52 ±1.07	16.21 ± 1.32	0.806	0.425

**Statistically significant, S.D-Standard deviation, G-Genitals, PH-pubic hair*

Table 3. Comparison of tanner stages among male study subjects

	Males		
Tanner stages	**HIV-infected n=80(%)**	**Non HIV-infected n=80(%)**	**Total N=160(%)**
Genitals			
G1	16 (20.0)	4 (5.0)	20 (12.5)
G2	20 (25.0)	16 (20.0)	36 (22.5)
G3	16 (20.00)	26 (32.5)	42 (26.3)
G4	18 (22.5)	15 (18.7)	33 (20.6)
G5	10 (12.5)	19 (23.8)	29 (18.1)
	Chi Square=13.091,p-value=0.011*		
Pubic hair			
PH1	16 (20.0)	7 (8.8)	23 (14.4)
PH2	23 (28.8)	21 (26.2)	44 (27.5)
PH3	10 (12.5)	17 (21.2)	27 (16.9)
PH4	13 (16.2)	11 (13.8)	24 (15.0)
PH5	18 (22.5)	24 (30.0)	42 (26.2)
	Chi Square=6.451,p-value=0.168		

**Statistically significant G-Genitals, PH-pubic hair*

Table 4. Comparison of pubertal stage status in male study subjects

	Males		
Pubertal Stage Status	**HIV-infected n=80(%)**	**Non-HIV-infected n=80(%)**	**Total N=160(%)**
Recall			
Normal	73 (91.2)	75 (93.8)	148 (92.5)
Delayed	4 (5.0)	0 (0.0)	4 (2.5)
Precocious	1 (1.3)	2 (2.5)	3 (1.9)
Can't remember	2 (2.5)	3 (3.7)	5(3.1)
	Fishers exact= 3.955; p-value = 0.358		
Examination			
Normal	78 (97.5)	80 (100.0)	158 (98.8)
Delayed	2 (2.5)	0 (0.0)	2 (1.2)
	Fisher's exact p-value=0.497		

5. CONCLUSION

Pubertal onset occurred at a significantly later age in HIV-infected boys when compared to the non-HIV-infected boys. There is need to monitor pubertal development in HIV-infected boys so as to identify deviations from normal early and evaluate need for intervention.

CONSENT

Written informed consent was obtained from all the parents and caregivers of the study participants before enrolment into the study.

ETHICAL APPROVAL

Ethical approval was obtained from the Research Ethics Committee of the University of Port Harcourt Teaching Hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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