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Pubertal Development Pattern in HIV-Infected Girls in Port Harcourt, Southern 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: Unidentified and untreated pubertal abnormalities in HIV-infected girls may result in adverse psychosocial consequences as well as a reduced final adult height. The aim of the study was to determine the pubertal development pattern in HIV-infected girls receiving care in two tertiary hospitals in Port Harcourt, Southern Nigeria.
Materials and Methods: This was a comparative cross-sectional study involving 90 HIV-infected girls aged 10-18 years and 90 age, sex and socio-economic class matched non-HIV-infected girls.
Results: The mean age of pubertal onset in HIV-infected girls was 11.57±1.05 which was significantly higher than the mean age of 10.78±0.69 seen in the non-HIV-infected group (χ^2= 2.667, p=0.011). Sixty three (70%) of HIV-infected females had commenced puberty (Tanner stage 2 or above for breast development) compared to 83 (92.2%) of non-HIV-infected females. ($\chi^{2=}$16.277, p=0.003). Forty per cent (40%) of HIV-infected girls had attained menarche (40%) as against 52.2% in the comparison group but this difference was not statistically significant (χ^2=2.705, p=0.100). There was a higher prevalence of pubertal delay in HIV-infected girls (6.7%) compared to non-HIV-infected girls (1.1%).

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Conclusion: The mean age of Pubertal onset was significantly later in HIV-infected girls compared to non-HIV-infected. This could have negative implications for psychosocial and reproductive health in HIV-infected girls.

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

1. INTRODUCTION

Puberty is the biologic transition from childhood to adulthood [1]. It is characterized by the maturation of gametogenesis, secretion of gonadal hormones, and development of secondary sexual characteristics and reproductive functions [1,2]. Normal puberty results from the sustained mature activity of the Hypothalamic-Pituitary-Gonadal (HPG) axis. This central signaling is mediated by excitatory glutamate and inhibitory gamma aminobutyric acid (GABA) neurotransmitters and also modulated by nutritional signals such as leptin and ghrelin [3].

Pubertal onset results from a complex network in the hypothalamus which stimulates gonadotropin releasing hormone secretion leading to pituitary gonadotropin secretion. In girls, this leads to estradiol secretion which stimulates maturation of the ovarian follicle in addition to the development of secondary sexual characteristics [3-5]. The Tanner staging method is the most commonly used method for pubertal assessment. In girls, puberty commonly begins with breast development (thelarche) followed by the development of pubic hair, axillary hair and first menstrual bleeding (menarche) [1,6]. Pubertal development can be influenced by factors such as quality of nutrition, genetic make-up, presence chronic diseases as well as environmental exposures [3,5,7].

HIV/AIDS remain a global health concern with an estimated 39 million living with HIV at the end of 2022 majority of whom are in sub-Saharan Africa [8]. With greater access to Highly active antiretroviral therapy (HAART) and improvements in care, many perinatally HIV-infected children now survive into adolescence and adulthood [9].

Some previous authors have reported pubertal delays among HIV-infected children. This is defined as the absence of secondary sexual characteristics at an age that is ≥2 standard deviations above the mean for age and sex [10,11]. In girls, this translates to lack of breast development by age 13 years, lack of pubic hair by 14 years, lack of menarche by 16 years or greater than 5 years between thelarche and menarche [3,12]. The exact mechanism for pubertal delay in HIV-infected girls is largely unknown. Possible postulations include the chronic inflammation seen in HIV infection and its deleterious effect on the hypothalamic-pituitary-gonadal axis, repeated opportunistic infections and a possible growth hormone resistance in HIV-infected children [13].

Pubertal delays in HIV-infected girls may have negative impact on their psychosocial wellbeing as it may result in low self-esteem and depression [14]. It could also have negative implications for the future bone health, reproductive capacity and final adult height [15-17]. However, with early identification and intervention, HIV -infected girls will benefit from enhanced adherence to HAART, improvement in nutrition, psychosocial support and possibly low dose gonadal steroid hormone or growth hormone [13,18-20].

The aim of this study was to determine the pubertal development pattern in HIV-infected girls and compare with age, sex and socioeconomic class matched non-HIV-infected girls in Port Harcourt, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Design

This was a comparative cross sectional study conducted over a four month period (July 1st – October 31st, 2017).

2.2 Study Area

The study was carried out at the Paediatric departments of the University of Port Harcourt Teaching Hospital (UPTH) and the Rivers State University Teaching Hospital (RSUTH) which are both tertiary care hospitals. They are the major care centers for HIV-infected children in the city of Port Harcourt.

2.3 Study Population

The study subjects consisted of 90 HIV-infected girls age 10 -18 years recruited from the Paediatric ARV clinic while 90 non-HIV-infected girls who were matched for age, sex and socioeconomic class. The comparison group was recruited from the General children's outpatient clinic after excluding the presence of HIV through rapid diagnostic testing. Presence of other chronic diseases which may impact on pubertal development such as sickle cell anemia and congenital heart diseases were excluded through history and physical examination before recruitment into the study.

2.4 Study Procedure

A semi-structured interviewer administered questionnaire was used to obtain data on socio-demographic and pubertal characteristics. Menarche was determined by recall of the age of attainment. Furthermore, physical examination was conducted in a designated consulting room with good lighting and adequate privacy to determine the pubertal staging using the Tanner staging scale. This entailed using a set of pictorial diagrams to assess the breast and pubic hair development as follows:

2.4.1 Breast

B1- prepubertal breast; B2- breast and papillae elevated as small mound and areolar diameter increased; B3-breast and areolar enlarge and no contour separation; B4- areolar and papillae form secondary mound; B5-mature breast, nipple projects, areolar part of general breast contour.

2.4.2 Pubic hair

P1- preadolescent pubic hair; P2- Sparse and downy hair on medial border of labia; P3-Pigmented, coarse and more curled; P4-coarse, curly and abundant pubic hair; P5- adult feminine triangle spreading to medial surface of inner thigh.

Girls were classified as having begun puberty if they were Tanner stage 2 or more for breast and or pubic hair development and to have completed puberty when they were at Tanner stage 5 for breast and pubic hair development provided menarche had occurred.

2.5 Statistical Analysis

Statistical analysis was performed using IBM SPSS version 20.0 Results were presented as simple proportions using charts and tables. Comparison of mean ages of attainment of pubertal events in the HIV-infected and non-HIV-infected groups was done using the student t-test. Fisher exact test and Chi Square test were used in the comparison of proportions. Statistical significance was set at 95% confidence interval with p-value <0.05.

3. RESULTS

A total of 90 HIV-infected and 90 non-HIV-infected girls were involved in the study. The mean age of HIV-infected girls was 13.32±2.40 years while that of non-HIV-infected girls was 13.31±2.41 years (t=0.0279, p=0.9778).

Tables 1 and 2 show that the mean age of pubertal onset which was defined by onset of breast budding was significantly lower in non-HIV-infected girls in comparison to the HIV-infected ones. Onset of pubic hair development and menarche were also significantly earlier in non-HIV- infected girls when compared to the HIV-infected subjects.

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

	Females			
Pubertal event recall	**HIV-infected Mean age ± S.D (years)**	**Non-HIV-infected Mean age± S.D (years)**	**t**	**p-value**
Breast	11.37 ± 1.12	10.36 ± 1.13	4.312	0.0001*
Pubic hair	11.39 ± 1.44	10.59 ± 1.11	3.067	0.003*
Axillary hair	11.43 ± 2.05	11.14 ± 0.92	0.806	0.423
Menarche	12.82 ± 0.96	12.27 ± 0.66	2.911	0.005*

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

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

	Females			
Tanner stages	**HIV-infected Mean age ± S.D (years)**	**Non HIV-infected Mean age ± S.D (years)**	**t**	**p-value**
Breast				
B1	11.40 ±2.01	10.34 ± 1.66	1.281	0.209
B2	11.57±1.05	10.78 ± 0.69	2.667	0.011*
B3	13.06 ±1.94	12.25 ± 1.03	1.754	0.087
B4	14.62 ±1.39	13.93 ± 0.83	1.574	0.128
B5	16.39 ± 1.67	16.36 ± 1.41	0.063	0.951
Pubic Hair				
PH1	11.50 ± 2.35	10.40 ± 1.66	1.074	0.297
PH2	11.74 ± 1.51	10.91 ± 0.71	2.281	0.027*
PH3	12.56 ± 1.57	12.28 ± 1.19	0.623	0.544
PH4	14.30 ± 1.55	13.36 ± 1.01	1.945	0.062
PH5	16.16 ± 1.57	16.13 ± 1.55	0.063	0.946

**Statistically significant; S.D-Standard Deviation; B-Breast; PH-pubic hair*

Table 3. Comparison of tanner stages among female Study subjects

	Females		
Tanner stages	**HIV-infected n=90(%)**	**Non HIV-infected n=90(%)**	**Total N=180(%)**
Breast			
B1	27 (30.0)	7 (7.8)	34 (18.9)
B2	18 (20.0)	18 (20.0)	36 (20.0)
B3	15 (16.7)	26 (28.9)	41 (22.8)
B4	13 (14.4)	14 (15.5)	27 (15.0)
B5	17 (18.9)	25 (27.8)	42 (23.3)
	*Chi Square=16.277, p-value=0.003**		
Pubic hair			
PH1	11 (12.2)	7 (7.8)	18 (10.0)
PH2	29 (32.2)	20 (22.2)	49 (27.2)
PH3	18 (20.0)	19 (21.1)	37 (20.6)
PH4	12 (13.4)	16 (17.8)	28 (15.5)
PH5	20 (22.2)	28 (31.1)	48 (26.7)
	Chi Square=4.474, p-value=0.346		

**Statistically significant; B-Breast; PH-pubic hair*

Although a greater proportion of Non-HIV-infected girls had attained puberty in comparison to the HIV-infected girls as shown in Fig. 1, this difference was not statistically significant (χ^2=2.705, p=0.100).

Table 3 shows that a greater proportion of the non-HIV-infected participants were found to be in more advanced Tanner stages of breast development in comparison to the HIV-infected group (χ^2=16.277, p=0.003).

Pubertal delay was significantly more common in the HIV-infected girls when compared to the non-HIV-infected group.

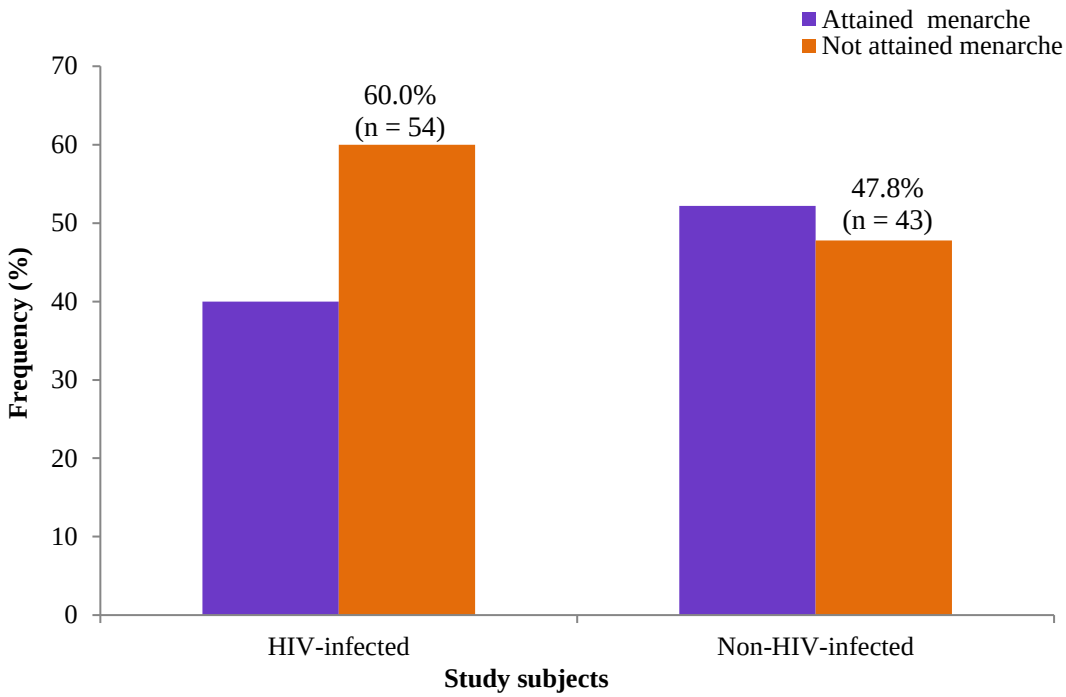

Fig. 1. Proportion of female study subjects who have attained menarche

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

	Females		
Pubertal Stage Status	**HIV-infected n=90(%)**	**Non HIVinfected n=90(%)**	**Total N=180(%)**
Recall			
Normal	78 (86.7)	89 (98.9)	167 (92.8)
Delayed	12 (13.3)	1 (1.1)	13 (7.2)
	*Fisher's exact p-value=0.002**		
Examination			
Normal	84 (93.3)	89 (98.9)	173 (96.1)
Delayed	6 (6.7)	1 (1.1)	7 (3.9)
	Fisher's exact p-value=0.118		

**Statistically significant*

4. DISCUSSION

The mean age of pubertal onset among HIV-infected girls in our study was 11.57±1.05 years. This finding compares favorably with the 11.7 years reported by Szubert *et al,* [13] among HIV-infected females in Uganda and Zimbabwe. It is however higher than that reported in some studies done in the United States of America [18,21] Our finding in this regard also differs from that reported by Mbwile, [22] in Tanzania where the median age of pubertal onset in HIV-infected girls was reported to be 13 years. The differences in age of pubertal onset between our study and those in comparison may reflect variations in environmental and nutritional factors which may influence pubertal onset among the different children studied.

On physical examination, the proportion of HIV-infected females who had attained puberty were significantly lower than that of non-HIV-infected females. Similar difference in proportion between HIV-infected and non-HIV-infected children has been reported in previous studies. 9,10,93 Whereas 70% of HIV-infected girls in the index study had attained puberty, Mbwile, [22] reported lower proportions in Tanzania where only 49% of HIV-infected females were found to have attained puberty. The proportion of HIV-infected females who had attained puberty in this study was also higher that reported by Iloh *et al,* [23] in

Enugu. This may be because the subjects in the present study were aged 10-18 years whereas the studies by Mbwile, [22] and Iloh *et al,* [23] included younger children from eight years of age.

Regarding age at completion of puberty, this study found no statistically significant difference between the mean ages of HIV-infected adolescents at completion of puberty and that of non-HIV infected adolescents. This concurred with the finding by Iloh *et al,* [23] in Enugu.

Breast development was the first sign of pubertal onset noted in our study. This is similar to findings by most authors in previous studies. However, the findings by Ilo *et al*, [23] contrasts from ours in this regard as pubic hair development was the first sign of pubertal development reported in their study. The reason for this disparity is unclear.

Concerning menarche, there was no statistically significant difference in the proportion of HIV-infected and non-HIV-infected females who had attained menarche in the present study. This similarity may be attributed to the benefits of nutritional advice given to the two population of girls in the hospital since the index study is a hospital-based study. This finding also agrees with that by Iloh *et al,* [23] in Enugu. Nevertheless, the proportion of HIV-infected females who had attained menarche in this study was higher than the 20.8% reported by Mbwile, [22] in Tanzania. This difference in proportions may be attributed to the fact that the study by Mbwile, [22] included younger children from eight years of age.

This study also showed that the mean age at menarche in HIV-infected females was significantly higher than that for non-HIV-infected females. Other studies done elsewhere have demonstrated similar differences The mean age at menarche in the index study was comparable to those reported by Iloh *et al*, [23] in Enugu and Bellavia *et al,* [24] in the United States of America. It was however lower than that reported by Mbwile, [22] in Tanzania.

Evaluation of pubertal stage status showed that majority of HIV-infected girls in the present study had normal pubertal development both by recall and physical examination. However, pubertal delay was more common in HIV-infected girls compared to the non-HIV-infected ones using the recall method. This may be attributable to the negative effect of immunosuppression on the hypothalamic-pituitary-gonadal axis. The higher prevalence of pubertal delay seen among HIV-infected girls corroborates findings by Ilo *et al*, [23] in Enugu and Buchacz *et al,*[18] in the USA.

The proportion of HIV-infected girls in the present study who had pubertal delay was 13.3%. This was lower than the 22.2% reported by Shadab *et al*, [25] in India and 56% reported by Szubert *et al*, [13] in Uganda and Zimbabwe. It was however higher than the 6.25% reported by Iloh *et al*, [23] in Enugu, Nigeria. The variations in proportion of HIV-infected girls with pubertal delay seen among the different studies in comparison may be explained by differences in other factors that influence pubertal development such as nutrition, socioeconomic status and environmental exposures.

5. CONCLUSION

HIV-infected girls attained puberty at significantly later ages compared to the non-HIV-infected girls. There is need to monitor pubertal development in HIV-infected girls so that abnormalities can be identified early and necessary interventions given.

CONSENT

Written informed consent was obtained from all the parents and caregivers of all participating children 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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