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Original Article

Psychosocial dysfunction and delayed sexual development among adolescents living with HIV in Lagos, Nigeria.

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Abstract

Background: With increasing survival following the use of antiretroviral therapy, adolescents living with Human Immunodeficiency Virus (ALHIV) could have complications such as delayed puberty and psychological complications. In Nigeria, there is limited data on the association between delayed sexual maturation and psychosocial dysfunction in ALHIV. The objective of this study was to determine the prevalence and the association between delayed sexual development (DSD) and psychosocial dysfunction (PSD) in ALHIV and compare it with uninfected adolescents.

Methodology: This was a cross-sectional study conducted at the Lagos University Teaching Hospital (LUTH), Nigeria and it involved 144 ALHIV and an equal number of HIV-negative controls who were matched for age, sex and social class. Information was obtained from participants using interviewer-administered questionnaires; their stages of sexual development and their psychosocial function were assessed using Tanner staging criteria and the Paediatric Symptom Checklist tool respectively. Data were analysed using the Statistical Package for Social Sciences software version 23.

Results: The mean (±SD) age of ALHIV and the HIV-negative controls was 14.8 (±3.0) and 14.8 (±2.9) years respectively. All the ALHIV were on HAART and 99.3% were in clinical stage 1. There was no significant difference between the prevalence of DSD among the ALHIV (9.4%) and the HIV-negative controls (6.4%) (p= 0.402). The prevalence of PSD in ALHIV and HIV-negative controls were 4.9% and 5.6% respectively (p=0.791). There was no significant association between PSD and DSD in both groups of study participants (p=0.459 and p=0.301).

Conclusion: The prevalence of PSD and DSD were low and similar among adolescents with and without HIV, and no association was found between PSD and DSD. However, routine screening of adolescents for PSD should be practised for early identification and prompt management where indicated.

Keywords: Psychosocial Dysfunction; Delayed Sexual Development; Human Immunodeficiency Virus; Tanner Staging.

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Introduction

Human immunodeficiency virus (HIV) infection is a global disease of public health concern and a leading cause of morbidity and mortality, especially in sub-Saharan Africa.[1] Nigeria accounts for 9% of the global population living with HIV.[1,2]The Joint United Nations Programme on HIV/AIDS (UNAIDS) in the 2021 national review estimated that approximately 170,000 children (aged 0 – 14 years) and about 1,900,000 adolescents and adults (up to 15 years and above) were living with HIV infection in Nigeria.[3]The report also showed that HIV infection was responsible for the deaths of 33,000 adults and 17,000 children.[3]

The diagnosis of HIV infection in a child or adolescent impacts not only the physical health but also the mental, emotional and social life of the developing child.[4] The introduction and increasing use of antiretroviral therapies have translated into the survival of more of these children into adolescence and adulthood, thereby increasing the incidence of long-term complications of the infection.[5]HIV infection in adolescents is also associated with severe morbidities, including neurologic, cardiovascular, pulmonary, renal, musculoskeletal and haematologic complications, all of which impact the physical health of the child.[6]Globally and in Nigeria, one of such reported complications is delayed puberty which has been observed to be more prevalent in adolescents living with HIV compared to their HIV-uninfected counterparts.[7,8,9,10,11]HIV infection is also associated with psychological and psychosocial dysfunctions in adolescents, especially when it is diagnosed in childhood and adolescence.[2,4,12,13]

Potentially, a delay in sexual development could have a significant psychological impact on these adolescents who may already be experiencing challenges with relating with peers as a result of the diagnosis, especially at a critical point in their social development.[14] Poor sexual development may result in poor self-esteem which may worsen mood and psychosocial problems such as eating disorders, depression, social withdrawal, isolation, declining academic performance, teasing and bullying by peers.[9] The study aimed to determine the prevalence and the association between psychosocial dysfunction and delayed sexual development in ALHIV.

Materials and Methods

This was a cross-sectional study carried out over a 5-month period at the Paediatric HIV clinic of the Lagos University Teaching Hospital (LUTH), Lagos Nigeria. Lagos is in the Southwestern part of the country. Lagos University Teaching Hospital is one of the tertiary hospitals in the state. It is a multi-specialist hospital and serves as a referral center providing healthcare services to individuals within the state and its neighbouring states. It also provides comprehensive healthcare for people living with HIV including adolescents.

The study participants were adolescents living with HIV (ALHIV) attending the Paediatric HIV clinic in LUTH. The control group included age, sex and socio-economic class-matched HIV-negative adolescents who attended the paediatric general outpatient clinics during the study period. They were screened and tested negative for HIV before recruitment.

Adolescents who had co-morbidities unrelated to HIV infection, that could affect growth and development e.g. sickle cell anaemia and congenital heart diseases, were excluded from the study.

Ethical approval was obtained from the Health Research and Ethics Committee of Lagos University Teaching Hospital (ADM/DCST/HREC/APP/3094). Written informed consent was obtained from the parents/caregivers of the study participants as well as those adolescents up to 18 years and above, and assent was obtained from the other adolescents.

A minimum sample size of 288 was obtained using the formula for a comparative study involving proportions.[15]Participants who met the eligibility criteria were recruited consecutively until the sample size was reached.

Data Collection

An interviewer-administered questionnaire was used to obtain information on the socio-demographic characteristics of the study participants as well as the clinical history of the ALHIV. Other clinical information such as names and duration on anti-retroviral drugs, latest CD4 count, and viral load were retrieved from their medical records. The participants were examined to determine their stages of sexual development using the Tanner staging criteria and those with delayed sexual development were identified. Delayed sexual development was defined clinically as the absence of secondary sexual characteristics by age 13 years in girls or age 14 years in boys[16] i.e. Tanner stage 1 for breast and pubic hair development in girls up to 13 years, and Tanner stage 1 for genital and pubic hair development in boys up to 14 years.

Assessment of their psychosocial function was done using the Paediatric Symptom Checklist (PSC).[17] The standard youth-completed PSC form consists of 35 items. Each item was rated as Never (scored 0), Sometimes (scored 1), and Often (scored 2). The total score was calculated by adding 35 individual scores, such that the total score was 0 to 70. A total score of 30 and above was indicative of the presence of psychosocial dysfunction while a score less than 30 indicated the absence of psychosocial dysfunction.

Data analysis

Data were analysed using Statistical Package of Social Sciences Version 23 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized using frequencies and percentages while quantitative variables were summarized using means/median and standard deviation/ interquartile range. Fisher's exact test was used to examine for association between delayed sexual development and psychosocial dysfunction among the participants. P-value < 0.05 was considered statistically significant at 95% confidence interval.

Results

Socio-demographic characteristics of the participants

The mean age of all participants was 14.8 ± 2.9 years. In both groups, the least populated group was the age range of 14 to 16 years (26.4%). Over one-quarter (27.1%) of participants with HIV infection reported that their parents were living apart compared to 6.3% of the controls who reported the same ($p < 0.001$). The most common reason provided for parents not being together was the death of a parent seen in 85.4% of all participants living with a single parent. Other reasons were the separation of parents (10.4%) or never married (2.1%). (Table 1)

Table 1: Socio-demographic characteristics of study participants

Variables	HIV-positive	HIV-negative	χ^2	p-value
Age group(years)				
10 – 13	54 (37.5)	53 (36.8)		
14 – 16	38 (26.4)	38 (26.4)	0.019	0.991
17 – 19	52 (36.1)	53 (36.8)		
Mean age ± SD	14.8 ± 3.0	14.8 ± 2.9	t = 0.121	0.903
Gender				
Male	72 (50.0)	72 (50.0)		
Female	72 (50.0)	72 (50.0)	0.000	1.000
Both parents living together				
Yes	105 (72.9)	135 (93.8)		
No	39 (27.1)	9 (6.3)	22.500	< 0.001*
Orphan status				
Single	22 (15.3)	4 (2.8)		
Double	12 (8.3)	2 (1.4)	22.766	<0.001*
Both parents alive	110 (76.4)	138 (95.8)		
Socio-economic class				
High	49 (34.0)	57 (39.6)		
Low	95 (66.0)	87 (60.4)	0.955	0.328

*: Statistically significant,

Clinical characteristics of participants with HIV infection

Among the ALHIV in this study, the mean duration of HAART use was 9.9 ± 4.2years; about 85% of the adolescents had been on HAART for more than five years and more than half of the adolescents on HAART (59.0%) were on the TDF/3TC/DTG combination. The most severe clinical stage documented in their case records was stage 4. A small proportion of the adolescents (6.3%) had non-suppressed viral load (≥1000copies/mm^3) while 75% of them had a high CD4 count, up to 500cells/mm^3.This is shown in Table 2.

Table 2: Clinical characteristics of participants with HIV infection.

Variables	Frequency (%)
HAART drugs	
Protease inhibitor-based combination	49(34.0)
Non-protease inhibitor-based combination	95(66.0)
Duration of using ART (years)	
≤ 5 years	21 (14.6)
>5 years	123 (85.4)
Mean ± SD	9.9 ± 4.2
Viral load, copies/mm^3	
< 1000	135 (93.8)
≥ 1000	9 (6.3)
Median (IQR)	20.0 (20.0 – 30.1)
CD4+ count, cells/mm^3	
< 500	35 (24.3)
≥ 500	109 (75.7)
Median (IQR)	717.0 (502.5 – 1031.0)

Most severe clinical stage documented	
1	59 (41.0)
2	32 (22.2)
3	37 (25.7)
4	16 (11.1)

IQR: interquartile range
Protease inhibitor-based combination: ABC/3TC/LPV/r, TDF/3TC/ATV/r, ABC/3TC/ATV/r
Non-protease inhibitor-based combination: TDF/3TC/DTG, ABC/3TC/DTG, AZT/3TC/NVP, AZT/3TC/EFV
3TC= Lamivudine, ABC=Abacavir, AZT= Zidovudine, DTG=Dolutegravir, EFV=Efavirenz, ATV/r=Atazanavir/ritonavir, LPV/r= Lopinavir/ritonavir, NVP=Nevirapine, TDF=Tenofovir

Distribution of stages of secondary sexual characteristics in study participants

Among the female adolescents, more of the ALHIV were in the prepubertal stage of breast development compared to the HIV-negative group (22.2% and 13.9% respectively) while 61.1% of the HIV-negative females were in the later stages (4 and 5) of breast development compared to 33.4% of the HIV-positive females. The difference in the stages of breast development for the two groups was statistically significant (p=0.013). Also, 84.7% of the uninfected females had attained menarche compared to 72.2% of the females living with HIV, however, this difference was not significant(p=0.068). Table 3.

Table 3: Distribution of stages of breast development and menarche in female participants

Variables	HIV-positive (n =72) n (%)	HIV-negative (n = 72) n (%)	Total	Test statistic	p-value
Breast development					
Tanner breast stage					
Stage 1	16 (22.2)	10 (13.9)	26 (18.1)		
Stage 2	14 (19.4)	6 (8.3)	20 (13.9)	$\chi^2 = 12.756$	0.013*
Stage 3	18 (25.0)	12 (16.7)	30 (20.8)		
Stage 4	12 (16.7)	16 (22.2)	28 (19.4)		
Stage 5	12 (16.7)	28 (38.9)	40 (27.8)		
Menarche					
Yes	52 (72.2)	61 (84.7)	113 (78.5)	$\chi^2 = 3.330$	0.068
No	20 (27.8)	11 (15.3)	31 (21.5)		
Mean ± SD age (years) at menarche	13.2±1.8	12.8±1.3		t=1.505	0.135
Mean ± SD age (years) at the onset of breast development	11.8±2.1	11.8±1.7		t =0.174	0.862

*: statistically significant

Unlike the female adolescents, 25% of the male controls were in the prepubertal stage of genital development compared to the proportion (19.4%) of HIV-positive male adolescents. The same number of male participants were in the tanner stages 4 and 5 of genital development in both groups (p= 0.330). (Table 4)

Table 4: Distribution of stages of genital development in male participants

Variables	Cases (n =72) n (%)	Controls (n = 72) n (%)	Total	Test statistic	p-value
Genital development					
Tanner genitalia stage					
Stage 1	14(19.4)	18(25.0)	32(22.2)	$\chi^2 = 4.609$	0.330
Stage 2	7(9.8)	12(16.7)	19(13.2)		
Stage 3	19(26.4)	10(13.9)	29(20.1)		
Stage 4	14(19.4)	14(19.4)	28(19.4)		
Stage 5	18(25.0)	18(25.0)	36(25.0)		
Mean ± SD age (years) at the onset of genital development	13.0±1.6	12.1±1.6		t=2.920	0.004*

*: statistically significant,

From Table 5, 22.2% of the ALHIV and 16.0% of the HIV-negative adolescents were in the prepubertal stage of pubic hair development, however, the difference was not statistically significant (p= 0.056).

Table 5: Distribution of stages of pubic hair development in study participants

Variables	Cases (n= 144)	Control (n= 144)	Total	Test statistic	p-value
Pubarche					
Tanner pubic hair stage					
Stage 1	32 (22.2)	23 (16.0)	55 (19.1)	$\chi^2 = 9.209$	0.056
Stage 2	15 (10.4)	20 (13.9)	35 (12.2)		
Stage 3	31 (21.5)	17 (11.8)	48 (16.7)		
Stage 4	25 (17.4)	26 (18.1)	51 (17.7)		
Stage 5	41 (28.5)	58 (40.3)	99 (34.4)		
Mean ± SD age (years) at the onset of pubarche	11.7 ± 1.57	11.6 ± 1.7		t= 0.877	0.381

Prevalence of psychosocial dysfunction and delayed sexual development in study participants.
Among the study participants, the prevalence of delayed sexual development (DSD) was determined in female adolescents aged ≥13 years and in male adolescents aged ≥14 years, in keeping with the definition of delayed puberty in the current study. The total number of ALHIV that were assessed for DSD was 106 while the total number in the control group was 110. The prevalence of DSD among ALHIV and HIV-negative adolescents was 9.4% and 6.4% respectively (p=0.402).

In all the study participants, the prevalence of psychosocial dysfunction (PSD) using the Paediatric Symptom Checklist (PSC) was 5.2%. The prevalence of PSD in the control group was slightly higher than the prevalence in the ALHIV, however, the difference was not statistically significant. (5.6% vs 4.9% respectively (p = 0.791)

Association between delayed sexual development and psychosocial dysfunction in study participants
None of the ALHIV who had delayed sexual development (DSD) had psychosocial dysfunction (PSD); only one of the HIV-negative adolescents with DSD had PSD. There was no statistically significant association between DSD and PSD in the ALHIV (p = 0.459). A similar pattern was noted in the HIV uninfected group (p = 0.301). (Table 6)

Table 6: Association between delayed sexual development and psychosocial dysfunction in study participants.

Variables	Psychosocial dysfunction		Test statistic	p-value
	No	Yes		
HIV-positive, n = 144 n (%)				
Delayed sexual development				
Yes	10 (100.0)	0 (0.0)	**0.549	0.459
No	127 (94.8)	7 (5.2)		
HIV-negative, n = 144 n (%)				
Delayed sexual development				
Yes	6 (85.7)	1 (14.3)	**1.069	0.301
No	130 (94.9)	7 (5.1)		

**Fisher's exact

Discussion

The prevalence of PSD in ALHIV (4.9%) was comparable to that among uninfected adolescents (5.6%). This similarity was unanticipated since it was assumed that the presence of HIV infection may increase the risk of PSD in adolescents.[18] The lack of a predisposition found in the present study differs from the higher prevalence of PSD reported in previous studies in South-south[12]and Northwest Nigeria[13]which reported a higher prevalence of depression and psychological complications in ALHIV. In these studies, however, not all of the HIV-positive adolescents had commenced HAART and some were in the advanced stages of the disease.[12,13] More advanced disease may predispose affected children to mood and psychological disorders. In the current study, the ALHIV had been on anti-retroviral therapy with a mean duration of about 10 years and almost all were in clinical stage I at the time of recruitment. This supports the beneficial role of HAART in mitigating the physical and psychosocial complications (e.g depression) of HIV.[19] Furthermore, the lower prevalence in this study in contrast to that reported by Lawan *et al*[13] could also be due to the unmarried status of all the participants in the current study. The additional burden of managing a home or losing a spouse as seen in their study can lead to or worsen psychosocial impairment.[20]

Louthrenoo *et al* in Thailand[18] and Bomba *et al* in Italy[21] also reported a higher prevalence of PSD in ALHIV. Unlike the Y-PSC questionnaire that was used in the current study, these studies employed the use of other tools to assess the participants for PSD; this might account for the difference in the results. The higher number of adolescents who lived with either or both biological parents in this study could explain the lower prevalence of PSD in the current study unlike the report from the Thailand[18] where a fewer number of adolescents lived with their biological parents. This could be because lack of care, love and attention due to the absence of one or both parents could lead to negative psychological effects on children.[22]

Among the non-infected adolescents, the prevalence of PSD in this group is comparable to the prevalence of depression reported by Bankole *et al*[12] among the HIV negative participants in their study. However, Bista *et al*[23]in a school based study in Nepal found a higher prevalence of psychosocial dysfunction among adolescents. The difference in prevalence could be due to the larger number of adolescents in the Nepal study as well as differences in geographical distribution.

The current study found a higher prevalence of DSD among the ALHIV but the difference was not significant. This prevalence is comparable to the finding by Iloh *et al* [9] in Southeast Nigeria. They reported that 6.25% of the female adolescents older than 13 years had no evidence of breast or pubic hair development.[9] Even though this study and Iloh *et al*[9] employed the use of the standard pictures by Tanner for pubertal staging, the lower prevalence in the current study could be explained probably by the higher number of participants on HAART (100% vs 86%) and their longer duration on HAART.

David *et al* [10] and Ndiokwelu *et al*[11]in Nigeria also reported delay in sexual development among female and male HIV-positive adolescents respectively compared to non-infected controls as most of the adolescents with HIV were in the early Tanner stages of breast and genital development compared to the controls.

In a longitudinal cohort study done in America,[7] a low prevalence (4.1%) of delayed pubertal onset among adolescents who were perinatally infected with HIV was also reported. Early commencement of antiretroviral drugs could have been responsible for the low prevalence of delayed puberty obtained in their study. Conversely, a higher prevalence of pubertal delay (21%) was reported by McHugh *et al*[24] among adolescents with HIV infection. All the participants were diagnosed late with the infection and were all HAART naïve. These reasons could be responsible for the higher prevalence of pubertal delay as well as the other co-morbidities reported in the study.[24]

For the HIV-negative adolescents, most of them were in the later stages of sexual development as found in other studies[10,11,25]However, this was not the case from the report by Iloh *et al*.[9] This could be because of the younger aged participants recruited in their study.[9]

The current study found no statistically significant association between PSD and DSD in adolescents with and without HIV infection. Since delayed sexual maturation has been previously noted to have a profound psychosocial impact on adolescents, and even continue into adulthood,[26,27] it is crucial to further explore this subject in subsequent studies to identify and perhaps mitigate its occurrence, especially in adolescents living with HIV infection.

Conclusion

The prevalence of delayed sexual development and psychosocial dysfunction in ALHIV on anti-retroviral therapy was not significantly different from the prevalence in HIV-negative adolescents. No association was found between delayed sexual development and psychosocial dysfunction in ALHIV.

Limitations

Since this was a cross-sectional study, the exact timing of the onset and completion of a particular pubertal Tanner stage could not be established. Additionally, this study was conducted in a single state, which limits the generalizability of the findings to adolescents in other states in Nigeria.

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