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Assessment of the impact of HIV infection on the hypothalamic-pituitary-ovarian axis and pubertal development among adolescent girls at a tertiary centre in Zimbabwe: a cross-sectional study

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Abstract

Background Proper planning of reproductive health needs for HIV-infected adolescents requires a clear understanding of the effects of HIV infection on adolescents' pubertal development.

Objective To assess the effects of HIV infection on the hypothalamic-pituitary-ovarian (HPO) axis, ovarian reserve and pubertal development in adolescent girls at a tertiary hospital in Zimbabwe.

Methods This was a cross-sectional survey of HIV-infected adolescent girls aged 10–19 years, with available CD4 + count results at a tertiary hospital in Zimbabwe. Consecutive sampling was used to select study participants. Pubertal milestones were assessed using the age of menarche and Tanner stage for breast and pubic hair development. Growth was assessed using World Health Organisation growth charts. The HPO axis was evaluated by measuring serum follicular stimulating hormone (FSH), luteinising hormone (LH) and estradiol. The ovarian reserve was assessed in adolescents above 18 years of age by measuring the serum anti-mullein hormone (AMH) levels. Data were analysed in STATA version 13.0, and the results are presented as mean (SD) or median (quartiles) and proportions, as appropriate.

Results One hundred and one (101) HIV-infected adolescents were recruited for the study. Menarche, thelarche and pubarche were delayed in 15.9%, 28.6% and 46.8% of the adolescents, respectively. A total of 59.4% had moderate to severe stunting, and 53.5% were either overweight or obese. Most participants had normal serum FSH, LH, and estradiol levels, and there was no association between these hormone levels and growth indicators. The serum AMH levels were reduced in 24.1% of the adolescents. There were no significant differences in the hormonal levels and pubertal development between the WHO CD4 classes.

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Conclusion HIV infection is associated with stunted growth and delayed sexual maturation with an intact HPO axis in the majority of adolescents. There was no association between growth indicators and FSH and LH levels. The degree of HIV immunosuppression had no significant impact on the HPO axis and pubertal development. A larger study is needed to assess the impact of HIV infection on ovarian reserve.

Trial registration : This protocol was approved by the Medical Research Council of Zimbabwe (MRCZ) (reference number MRCZ/A/1730).

Keywords HIV, Adolescent girls, Hypothalamic-pituitary-gonadal axis, Ovarian reserve, Tertiary hospital, Zimbabwe

Background

Studies performed in Africa have shown that as the human immunodeficiency virus (HIV) epidemic has matured, the long-term survival of HIV-infected infants into adolescence is no longer a rare phenomenon [1, 2]. As of 2019, 78% of HIV-infected adolescents were receiving HIV care services, which was a significantly lower percentage than that for adults [3]. In 2021, 77,300 Zimbabwean adolescents aged 10 to 19 years were living with HIV [4]. As of 2023, ART coverage among adolescents was 75%, primarily due to a failure to locate children living with HIV and stigma resulting in these adolescents not presenting for treatment [5]. Despite the increase in the number of HIV-infected adolescents, most HIV clinical trials in Africa have concentrated on antiretroviral treatment (ART)-related outcomes in children and young adults [6, 7], and those that have assessed endocrine function have not measured changes in hormonal levels.

Zimbabwe succeeded in reducing the incidence of HIV infection in adults, with the number of newly infected people declining from 73,000 in 2010 to 25,000 in 2020, a 66% decline [8]. However, poorly controlled HIV and acquired immunodeficiency syndrome (AIDS) are still among the most common causes of emergency admissions and in-hospital deaths among adolescents in Zimbabwe [9]. This shows that the burden of HIV infection in adolescents in Zimbabwe is still very high, and by the time of HIV diagnosis, most of them are severely immunosuppressed [10].

A study performed on Zimbabwean and Ugandan HIV-infected adolescents to assess sexual maturation using Tanner staging regarding the age of ART initiation showed that the mean age of ART initiation was 9.4 years and that delaying ART initiation significantly delayed sexual maturation [11]. In another study performed in Zimbabwe, stunting and being underweight were more prevalent at ART initiation among late-diagnosed adolescents, especially boys with perinatally acquired HIV infection, and those diagnosed late were particularly at risk of growth failure in puberty [12].

Several studies have documented delayed sexual maturation, growth and development among HIV infected compared to HIV-uninfected adolescents [13–15]. A study conducted in Nigeria identified lower growth parameters and pubertal delay among HIV-infected compared to HIV-uninfected adolescent girls [16]. Several physiological mechanisms have been attributed to the delayed growth and development in this group of adolescents. These include chronic inflammation, increased catabolism and immunosuppression. Delayed sexual maturation can be explained by reduced levels of the hormone leptin, secondary to poor nutrition and reduced energy reserves in chronic illness. This affects the hypothalamic-pituitary-gonadal axis negatively, leading to reduced pulsatile release of gonadotrophin releasing hormone (GnRH) and disruptions in pubertal development [17, 18].

HIV-infected adults with reasonable immunological and virological control rarely exhibit endocrine dysfunction [19], but those with severe HIV infection may be significantly affected [20]. If the same phenomenon is true for adolescents, there might be a need to screen for some endocrinopathies to ensure normal growth, development and sexual reproduction, especially in those with poorly controlled HIV infection. As these adolescents mature into adults, it is crucial to know whether HIV infection accelerates ovarian ageing. This will facilitate counselling and planning for the reproductive health needs of these adolescents. Serum anti-Mullerian hormone (AMH) levels are an accurate marker of ovarian reserve, and serum AMH levels are not influenced by the stage of the menstrual cycle [21]. This makes it easier to assess the ovarian reserve in clinical practice.

Limited research in Africa has assessed endocrine function by measuring hormonal levels. The paucity of knowledge regarding the effect of ART on endocrine function has hampered the ability to facilitate counselling and planning for the long-term reproductive health needs of this population. To fill this knowledge gap and enable proper planning of reproductive health services for this population, we undertook this study to assess the effect of HIV infection on reproductive endocrine function, pubertal development and ovarian reserve in adolescents between 10 and 19 years of age. To the best of our knowledge, this is the first study in Africa assessing endocrine function in HIV-infected adolescents by measuring hormone levels.

Methods

A cross-sectional survey was conducted between 22 July 2013 and 21 October 2013 at an HIV clinic at Parirenyatwa Group of Hospitals (PGH), the largest tertiary hospital in Zimbabwe. The study population comprised HIV-infected adolescent girls aged 10–19 attending the clinic.

In a study done in Zimbabwe, the prevalence of delayed pubertal development in HIV-infected adolescents was 73%; hence, a sample size of 101 allows estimation of this prevalence with a precision of 8.66%, assuming a 95% confidence interval [22]. Consecutive sampling was used to select the participants in the study. For adolescents below the age of 18 years, they signed an assent form and had their parents or legal guardians sign a consent form for them. Participants without signed assent or consent forms and those who were pregnant were excluded from the study due to possible alterations of hormonal levels in pregnancy. Those who were acutely ill were excluded due to difficulty in consciously signing the assent form and actively participating in the growth assessment process.

The study investigators collected the data through a face-to-face interview using a standardised data collection tool to capture the participants' sociodemographic, sexual, gynaecological, and medical history, including treatment adherence. HIV test results in the clinical records were used to confirm the HIV status of the adolescents. Adolescent girls had their breast and pubic hair examinations done by the investigators in the clinic. At the same time, growth was assessed by weight and height measurement using the standardised scale and stadiometer, respectively. Pubertal milestones were clinically assessed using the age of menarche, thelarche, and pubarche. Tanner stage was used for breast and pubic hair development. Tanner stage pictures were used during the assessment, and four investigators who attended the clinic were involved in adjudication when there was doubt [23]. They all had to reach a consensus for the agreed staging to be used. Menarche was assessed based on the participant's history. Growth was then assessed using WHO growth charts [24]. A CD4 + T lymphocyte count to determine the severity of HIV infection was repeated if the result in the clinical file was more than six months old and the immunological stage was documented [25]. The ovarian reserve of adolescent girls above the age of 18 years was measured by a one-time serum AMH measurement. The hypothalamic-pituitary-gonadal axis was assessed by measuring the following serum hormones: follicular stimulating hormone (FSH), luteinising hormone (LH) and estradiol (E_2). The outcome measures of interest were delayed pubertal milestones defined as the absence of first signs of pubertal development by 13 years, retarded growth defined by a body mass index z-score < -2, abnormal HPO axis hormones (FSH, LH and E2), and serum AMH levels defined as levels outside the normal range for age [26].

Blood samples were collected from adolescent girls and analysed for hormone levels using the mini Vidas by BioMerieux, VIDAS ® (2013). The assay, an enzyme-linked fluorescent assay, is highly specific for the target hormones. The process involves a "sandwich" technique where the hormone binds to antibodies on a device. A fluorescent substrate is added, and the intensity of the resulting fluorescence is measured to determine hormone concentration. The assay has a high sensitivity and specificity, ensuring accurate results.

Statistical analyses were performed in STATA version 13.0 (StataCorp, College Station, TX, USA). Descriptive statistics summarised baseline characteristics, growth metrics, pubertal milestones, and hormonal levels. A test for differences between the distribution of growth hormone levels and the median of the reference range for each age group was performed Continuous variables were expressed as mean (SD) or median (quartiles). Categorical variables were presented as counts and percentages. BMI and height-for-age z-scores were calculated using the methodology defined by [27] and implemented in STATA. The following categories for height for age (H/A) were adopted for classifying nutritional status: very low height for age ($Z < -3$), low height for age ($-3 < Z < -2$), and adequate height for age ($Z \geq -2$). The following were used for body mass index (BMI)/age: low BMI for age ($Z < -2$), adequate BMI for age ($-2 \leq Z < +1$), overweight ($+1 \leq Z < +2$) and obesity ($Z \geq +2$). A Chi-squared or Fisher exact test was used to evaluate the association between categorical variables. A sign rank test was done to compare the reference age and sample age for each Tanner stage. The Kruskal-Wallis rank sum test was performed to test for the association between the immunosuppression (CD4 count) level and hormonal levels. Fisher's Exact test was used to assess the association between as well as pubertal development and immunological stage. A p-value of <0.05 was considered statistically significant for all the statistical tests done.

Results

Summary of sociodemographic and ART data

A total of 101 participants were recruited for the study. The median age of the adolescents in the study was 15.33 years (IQR 13–18, range 10–19). All of them were single, and the majority (65.6%) were still in secondary school. 19.8% had both living parents, and the rest were single or double orphans. A total of 94.1% were not yet sexually active. All the adolescents in the study were HIV positive, and 90.1% of them were receiving antiretroviral therapy. The reported optimal adherence to antiretroviral treatment was low at 63.7.% defined as not missing two or more doses of drugs in a month, translating to

Table 1 Baseline participant characteristics and antiretroviral therapy (ART) history ($n = 101$)

Characteristic (N = 101)	*n* (%)
Median Age (years)*(Q1; Q3)*	15 *(11;19)*
Education	
No education	2(2.0)
Primary school	33(32.7)
Secondary school	66(65.3)
Parental status	
Both parents alive	20(19.8)
Maternal orphan	17(16.8)
Paternal orphan	20(19.8)
Double orphan	44(43.6)
Sexually active	
Yes	5(5.0)
ART history	
Current ART (Yes)	91(90.1)
Not on ART	10(9.9)*
Duration of treatment (months)*	
< 6	1(1.1)
6 - <24	13(14.3)
24 - <60	34(37.3)
> 60	41(45.1)
Unknown	2(2.2)
Self-reported adherence to ART (> 96%)*	
> 95%	58(63.7)
≤ 95%	13(14.3)
Defaulter	8(8.8)
Unknown	12(13.2)
The regimen of anti-retroviral drugs (N = 91) *	
1st line (nevirapine-based antiretroviral therapy)	77(84.6)
2nd line (Lopinavir/ritonavir-based antiretroviral therapy)	13(14.3)
Unknown	1(1.1)
Immunological stage	
CD4 + T lymphocyte count (cell/mm3) *	
Not significant immunosuppression > 500	49(48.5)
Mild immunosuppression 350–499	23(22.8)
Advanced immunosuppression 200–349	14(13.9)
Severe immunosuppression < 200	15(14.8)
Average CD4 + count *(Q1;Q3)*	497*(19;2160)*

* WHO CD4 + classification of immunosuppression in HIV infection [29]. Ten participants were not on HAART

> 96% adherence [28]. There were only 8.8% who were defaulters, defined by missing two or more consecutive clinic appointments for antiretroviral therapy. According to immunological staging, only 29.4% of patients had advanced and severe immunosuppression. Most of the patients in this study were still receiving first-line treatment (74%) (Table 1).

Table 2 Pubertal milestones among HIV-infected girls against Tanner staging (pubic hair and breast) and menarche. $^{**}p < 0.05$

Tanner stage		Delayed pubertal milestone	Age at pubertal milestone mean (2*SD range)	
	N	*n*(%)	Reference group	Study group
Breast*				
Tanner 2	15	3(20.0)	11.2(9.0-13.4)	13.1 (9.6–16.7)**
Tanner 3	13	2(15.4)	12.2(10.0-14.3)	13.6(11.0-16.3)**
Tanner 4	38	16(43.2)	13.1(10.8–15.4)	15.4(11.1–19.8)**
Tanner 5	33	7(21.0)	15.3(11.9–18.8)	17.0(13.3–20.7)**
Total	101	28(28.6)	11.2(9.0-13.4)	13.1 (9.6–16.7)**
p-value		0.113		
Pubic hair				
Tanner 2	16	1(6.3)	11.7(9.3–14.1)	12.9(10.6–15.3)**
Tanner 3	15	5(33.3)	12.4(10.2–14.6)	14.3(10.2–18.4)**
Tanner 4	40	21(52.5)	13.0 (10.8–15.1)	15.8(11.5–20.1)**
Tanner 5	23	17(73.9)	14.4 (12.2–16.7)	17.0(13.6–20.5)**
Total	101	44(46.8)	11.7(9.3–14.1)	12.9(10.6–15.3)**
p-value		< 0.001		
Menarche				
Yes	72	9(12.5)	13.5(11.4–15.5)	16.3(12.3–20.3)**
No	29	1(3.4)		

* 3 and 7 participants had missing data concerning the Tanner stages for breast and pubic hair, respectively

Summary of growth among HIV-infected girls against WHO growth charts for adolescents

Most of the adolescents were stunted; 32.7% and 26.7% had moderate and severe stunting, respectively, and only 40.6% had a normal height for age. Of all the participants, 44.5% had a normal BMI for age, 41.6% were overweight, 11.9% were obese and 2% had a low BMI.

Summary of pubertal milestones among HIV-infected girls according to tanner staging

Overall, the study participants had delayed sexual maturity ratings compared to their expected milestones for each age group (Table 2). Over a quarter (28.4%, Table 2) had delayed breast development. However, 19.6% (Table 2) of them had advanced breast development. Pubic hair development was delayed in 33.3% (Table 2) and advanced in 13.1% (Table 2). Menarche was delayed in 45.2% of the participants.

Summary of serum FSH, LH, estradiol and AMH levels

Most participants had normal serum FSH, LH, and estradiol levels. The serum AMH concentration was reduced in one-quarter of the patients (Table 3).

Comparison of hormone level with reference range

A test for differences between the distribution of growth hormone levels and the median of the reference range for each age group was performed. For FSH, only the

Table 3 Distribution of the proportion of participants with abnormal serum follicle-stimulating hormone, luteinizing hormone and anti-mullerian hormone levels by age

Age (years)	FSH			LH			AMH		
	Reference range (IU/L)	Abnormality		Reference range (IU/L)	Abnormality		Reference range (IU/L)	Abnormality	
		Low n(%)	High n(%)		Low n(%)	High n(%)		Low n(%)	High n(%)
10–12 (n = 11)	0.7–8.3	0(0.0)	0(0.0)	0.0-6.8	0(0.0)	2(18.1)	< 8.8	0(0.0)	0(0.0)
13–15 (n = 45)	1.0-9.1	3(6.7)	5(11.1)	0.3–23.0	4(8.9)	4(8.9)	0.9–9.5	0(0.0)	0(0.0)
16–17 (n = 16)	0.4–9.9	0(0.0)	3(17.7)	0.0-26.4	0(0.0)	2(11.8)	0.9–9.5	0(0.0)	0(0.0)
>=18 (n = 29)	1.7–21.5	1(3.5)	0(0.0)	1.0-95.6	4(13.8)	0(0.0)	0.9–9.5	0(0.0)	7(24.1)

Table 4 Distribution of the proportion of participants with abnormal serum estradiol hormone levels by tanner stage

Tanner stage	serum oestradiol levels		
		Abnormality	
	Reference range (pg/ml)	Low n(%)	High n(%)
1 (*n* = 2)	5–10	0(0.0)	2(100)
2 (*n* = 15)	5-115	0(0.0)	1(6.7)
3 (*n* = 13)	5-180	0(0.0)	1(7.7)
4 (*n* = 38)	25–345	5(13.2)	0(0.0)
5 (*n* = 33)	25–410	4(12.1)	0(0.0)

median of the study participants in the 18 + age group was significantly lower than the midpoint of the reference range (4.89 vs. 11.6, $p < 0.01$). The median LH values for our study participants were significantly lower than the midpoint of the respective reference ranges ($p < 0.05$). The median AMH value for the 18 + age group was significantly lower than the midpoint of the AMH reference range for the age group ($p < 0.001$) (Table 4)

Growth indicators (HA and BMI) association with reproductive hormones

A test for the correlation between growth indicators (HA & BMI) and reproductive hormones was performed. There was no association between FSH or LH and growth indicators. Higher BMI was associated with lower AMH values (rho = -0.427, $p = 0.023$). However, there was no association between AMH and HA.

Pubertal stage and immunological staging

Pubertal stage parameters (menarche, thelarche and pubarche) were statistically tested for association with the CD4 immunological stage using the Fisher's Exact test with a p-value of 0.05 and the Null hypothesis stating no association between the independent and dependent variables. The results showed that there was no significant association between the immunological stage and pubertal stages. The p values were 0.1541, 0.1987 and 0.4154 for pubarche, thelarche and menarche, respectively, indicating that the null hypothesis is not rejected.

Serum hormonal levels and immunological staging (CD4 + count)

A Kruskal-Wallis rank sum test was conducted to test the differences in the serum levels of FSH, LH, Estradiol and AMH levels between the four WHO immunological stages. The p values for each hormone were as follows.

FSH Kruskal-Wallis chi-squared = 0.61367, df = 3, p-value = 0.893.

LH Kruskal-Wallis chi-squared = 0.81793, df = 3, p-value = 0.8452.

E2 Kruskal-Wallis chi-squared = 1.7497, df = 3, p-value = 0.6259.

AMH Kruskal-Wallis chi-squared = 0.32619, df = 3, p-value = 0.955.

Since $p > 0.05$ for all hormones, therefore, we conclude that, with the available data, there are no significant differences in hormonal levels (dependent variable) of the HPO axis and ovarian reserve marker between the WHO CD4 classes of immunosuppression (independent variable).

Discussion

A total of 28.3% of the adolescents on treatment in our study reported less optimal adherence (< 95%) or defaulted treatment. Considering that this was self-reported adherence, actual adherence might be lower. We also found that 9.8% of adolescents were not receiving ART, which is not surprising because they were born during the time when Zimbabwe had high HIV prevalence rates and the prevention of parent-to-child transmission of HIV (PPTCT) programmes were not adequately established. Mortality from HIV was also very high, and as a result, 80.4% of these adolescents were either single or double orphans. One of the problems arising from being an orphan is poor treatment adherence due to a lack of proper societal support structures [30]. This is reflected by our results, which showed that a total of 14.2% of the patients were already on second-line treatment due to first-line treatment failure.

Despite reasonable immunological control of HIV, stunting remains a significant issue in HIV-infected adolescents [31]. In our study, moderate and severe stunting affected 32.7% and 26.7% of the adolescents, respectively.

Similar studies conducted in Senegal and Cameroon reported similar results, indicating significant stunting in HIV-infected individuals [31, 32]. Several studies have shown that ART is associated with faster weight compared to height gain and growth recovery in children living with HIV, both in LMICs and HICs [33, 34]. This is in keeping with our findings, which show that for all adolescents who were on treatment, only 2% were wasted. It has been shown that the long-term harmful impact of HIV in adolescents can be prevented by timely diagnosis and early ART initiation [12, 33]. We believe that since treatment is now widely available, less stunting will be realised among adolescents who will be on ART.

In this study, most adolescents had an intact HPO axis, as shown by their hormone profiles. Hormonal levels (FSH, LH and oestradiol) were normal in most participants. This finding suggested that the HPO axis mostly remained intact regardless of HIV infection in the participants. There was no association between HIV control and serum LH, FSH and E2 levels. This finding contradicts a study that showed increased LH, FSH, and E2 in women with good virological control of HAART [35]. Another study showed that HAART was associated with increased levels of E2 but without a change in FSH and LH [36]. FSH and LH levels can be as high as the common presentation, which is due to the well-documented primary hypogonadism in HIV, and can also be low due to pituitary infections or neoplasms in HIV [37]. HPO axis suppression in HIV-infected patients has not been well studied and is likely to be multifactorial [38]. Not many studies have been done to compare the HPO axis between HIV uninfected, infected (ART-naive) and those with reasonable virological control. In our case, we acknowledge that using HIV viral load rather than CD4 count as a measure of control would have been better. Unfortunately, it was not done due to financial constraints, as it was not yet widely available as a standard of care for monitoring treatment disease control in the public sector at the time of the study.

Accelerated ovarian ageing was seen in a quarter of the adolescents who were above the age of 18 and had reduced ovarian reserve. This was also observed in a study in India, which showed significant ovarian failure among HIV-infected women [38]. Further analysis of our data showed that for adolescents above the age of 18, there was no association between AMH and HA. Interestingly, higher BMI in this age group was associated with lower AMH values. This is in keeping with a longitudinal study and a recent systematic review, where obesity was associated with decreased AMH levels in HIV-negative women of reproductive age [39, 40]. Looking at this similar finding in studies with HIV-negative women compared to our own, it would appear as though HIV infection is not a confounder of ovarian ageing in adolescent girls. In addition, in our own study, there was no significant difference between the classes of immunosuppression and serum AMH levels. However, we refrain from making such a conclusion because of the low sample size of adolescent girls above 18. Instead, we recommend that larger longitudinal studies be done to explore the impact of HIV infection on ovarian reserve in HIV-infected adolescents further.

Our findings showed that there was delayed sexual maturity compared to the reference range. Breast, pubic hair development and menarche were delayed in 28.4%, 33.3% and 45.2% of the adolescents, respectively. This has also been shown in other African studies (11,16,30). In terms of HIV control, there was no association between HIV control amongst the infected adolescents and pubertal stage parameters in our study. The pathophysiology by which perinatal HIV infection affects the onset of puberty and sexual maturity is mainly unknown, which can limit intervention for the affected adolescents. Despite this, we still feel that our findings support the importance of counselling HIV-infected adolescents about pubertal delay to avoid anxiety and self-stigmatisation as they compare themselves to their peers. Surprisingly, 19.6% of the participants had advanced breast development, while pubic hair development was also advanced in 13.1% of the adolescents. To our knowledge, this has not been demonstrated in previous studies. We take into cognisance the limitation of the lack of a comparison HIV negative group in our study to firmly conclude this.

Strengths

To our knowledge, this is the first study in Africa to assess the HPO axis in HIV-infected adolescents by measuring hormone levels. Our findings can form a framework for future studies to explore and help address endocrine and possible fertility problems of HIV-infected adolescents. We believe our findings have not changed much since the last decade because adolescents living with HIV infection are still presenting late to health facilities in Zimbabwe and other LMICs, and no specialised clinics have been set up to address any possible endocrinological medical problems.

Limitations

We did not collect data on the WHO clinical stage of the participants at baseline and during the study. We also did not measure the HIV viral load of participants when the study was conducted due to financial constraints, which is a better indicator of disease control. We also did not have any HIV-negative adolescents as a control group. It is, therefore, challenging to attribute all the observed differences solely to HIV or possibly other non-HIV

confounding factors. We recommend future studies to explore this further.

Conclusion

This study found that HIV infection in adolescents is associated with stunted growth and delayed sexual maturation, with no association between HIV immunosuppression and deranged HPO axis or pubertal development. There is a need for a larger study to examine the impact of HIV infection on ovarian ageing in adolescents.

Abbreviations

AIDS	Acquired immunodeficiency syndrome
AMH	Anti-mullerian hormone
ART	Antiretroviral therapy
BMI	Body mass index
CD4	Cluster of differentiation
E2	Estradiol
FSH	Follicle-stimulating hormone
HIV	Human immunodeficiency virus
HPO	Hypothalamic-pituitary-ovarian
IQR	Interquartile range
LH	Luteinising hormone
LMIC	Low and middle-income countries
MRCZ	Medical Research Council of Zimbabwe
PGH	Parirenyatwa group of hospitals
PPTCT	Prevention of parent-to-child transmission
WHO	World Health Organisation

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Author contributions

Methodology– B.G, T. C and M.C Formal analysis and interpretation-– B. G, M.C, V. D, B. M and M. CWriting– original draft preparation-– B.GWriting– review and editing of the article - H.M, T. C and R. TFinal approval of the version to be published– All authors.

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Data availability

The raw data supporting the conclusions of this study has been made available by the authors within the manuscript, without undue reservation, to any qualified researcher.

Declarations

Ethics approval and consent to participate

This protocol was approved by the Medical Research Council of Zimbabwe (MRCZ) (reference number MRCZ/A/1730). Informed consent to participate was obtained from all participants, and consent was obtained from parents or legal guardians for those under the age of 16.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

Consent of publication

Not applicable.

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