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Original Research

Association Between Gonadal Hormone Levels and HIV Viral Load in Male Patients.

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Abstract

Background: Hypogonadism is an important endocrine complication among men living with HIV. Its pathogenesis is multifactorial and may involve chronic inflammation, altered body composition, comorbidities, medications, antiretroviral therapy and disturbances of the hypothalamic-pituitary-gonadal axis. The relationship between HIV viral load and gonadal hormone levels remains uncertain. *Aim:* To assess the association between gonadal hormone levels and HIV viral load among male patients living with HIV. *Materials and Methods:* This hospital-based cross-sectional study included 80 male patients living with HIV aged 18-70 years. Demographic, clinical and treatment-related information was collected using a structured proforma. Serum free testosterone, follicle-stimulating hormone (FSH) and luteinising hormone (LH) were measured. Participants were classified as having eugonadism, primary hypogonadism or secondary hypogonadism. HIV viral load was categorised as target not detected (TND) or more than TND. Quantitative variables were compared using Welch's *t* test or one-way analysis of variance, while categorical associations were assessed using the chi-square test. Effect estimates were reported with 95% confidence intervals, and P<0.05 was considered statistically significant. *Results:* Of the 80 participants, 49 (61.3%) had eugonadism, 23 (28.8%) had primary hypogonadism and 8 (10.0%) had secondary hypogonadism; thus, the overall prevalence of hypogonadism was 38.8%. The mean free testosterone level differed significantly among eugonadal, primary-hypogonadal and secondary-hypogonadal participants [10.25 (3.68), 3.37 (1.41) and 3.71 (1.76) pg/mL, respectively; F=47.18, P<0.001]. FSH also differed significantly across the three groups (P=0.035), whereas LH did not (P=0.136). Viral load was TND in 72 (90.0%) participants and detectable in 8 (10.0%). Free testosterone [6.39 (3.66) vs 7.75 (4.57) pg/mL; P=0.356], FSH [4.37 (2.87) vs 6.13 (5.42) mIU/mL; P=0.167] and LH [3.03 (2.85) vs 4.77 (2.98) mIU/mL; P=0.138] did not differ significantly between participants with detectable and TND viral loads. The prevalence of any hypogonadism was comparable between the detectable and TND groups (37.5% vs 38.9%; OR=0.94, 95% CI: 0.21-4.26; P=0.244). *Conclusion:* Hypogonadism was common among male patients living with HIV but was not significantly associated with viral-load status. Gonadal dysfunction may persist despite virological suppression and appears to be influenced by factors beyond viral replication alone. Symptomatic men living with HIV should undergo appropriate hormonal evaluation irrespective of their viral-load status.

Keywords: *HIV viral load; Hypogonadism; Free testosterone.*

Introduction

Human immunodeficiency virus (HIV) infection remains a major global public-health concern despite substantial improvements in diagnosis, antiretroviral therapy (ART), and viral suppression. Effective ART has transformed HIV infection from a rapidly progressive disease into a manageable chronic condition, resulting in increased survival among people living with HIV. Consequently, long-term metabolic and endocrine complications have become increasingly important determinants of morbidity and quality of life. Viral load is a key indicator of HIV replication, treatment response, disease progression, and risk of transmission. Persistent viraemia may promote systemic inflammation, immune activation, nutritional disturbances, and dysfunction of multiple endocrine organs [1].

Hypogonadism is one of the most frequently reported endocrine abnormalities among men living with HIV. It may manifest as reduced libido, erectile dysfunction, fatigue, loss of muscle mass, reduced bone mineral density, infertility, depressive symptoms, and impaired quality of life. The condition may be caused by primary testicular failure, characterised by reduced testosterone with elevated luteinising hormone (LH) and follicle-stimulating hormone (FSH), or secondary hypothalamic-pituitary dysfunction, characterised by reduced testosterone accompanied by low or inappropriately normal gonadotropin levels. Although the prevalence of severe hypogonadism has decreased during the ART era, testosterone deficiency continues to be reported in young and middle-aged men living with HIV [2].

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The pathogenesis of gonadal dysfunction in HIV is multifactorial. Direct effects of HIV, chronic inflammation, advanced immunosuppression, opportunistic infections, pituitary or testicular involvement, weight loss, chronic systemic illness, medications, substance use, ageing, and ART-related metabolic alterations may disturb the hypothalamic-pituitary-gonadal axis. Altered concentrations of sex hormone-binding globulin may also complicate interpretation of total testosterone, making free testosterone particularly relevant when assessing androgen status in men with HIV [3]. Sex steroid hormones may themselves influence immune activation and HIV pathogenesis, suggesting a potentially bidirectional relationship between hormonal status and virological activity [4].

Higher HIV viral load may reflect inadequate viral suppression and greater disease activity, both of which could contribute to reduced testosterone production or altered gonadotropin secretion. Previous investigations have reported associations between uncontrolled viraemia and low androgen levels, although findings have not been consistent across different populations and treatment settings [5]. Differences in age, ART exposure, nutritional status, disease stage, hormone-assay methods, and definitions of hypogonadism may partly explain these variations. Evaluation of free testosterone, LH, and FSH together with viral load may therefore provide a more comprehensive understanding of gonadal dysfunction among men living with HIV. The present study was undertaken to assess gonadal hormone levels and determine their association with HIV viral load in male patients attending a tertiary-care centre.

AIM
To assess the association between gonadal hormone levels and HIV viral load among male patients living with HIV.

OBJECTIVES
1. To estimate serum free testosterone, luteinising hormone, and follicle-stimulating hormone levels among male patients living with HIV.
2. To determine the HIV viral-load status of the study participants.
3. To evaluate the association between gonadal hormone levels, hypogonadal status, and HIV viral load.

Materials and Methods
Source of Data
The study data were obtained from male patients diagnosed with HIV who attended the outpatient department or were admitted to the Department of Medicine of hospitals affiliated with Bangalore Medical College and Research Institute (BMCRI), Bengaluru. Relevant demographic, clinical, treatment-related, and laboratory information was collected directly from participants and verified using their clinical and ART-centre records wherever available.

Study Design
A hospital-based cross-sectional analytical study was conducted. Gonadal hormone levels and HIV viral load were assessed during the study period, and their association was analysed without providing any study-related therapeutic intervention.

Study Location
The study was conducted in the Department of Medicine and affiliated hospitals of Bangalore Medical College and Research Institute, Bengaluru, Karnataka. Laboratory investigations were performed in the designated institutional laboratories and HIV viral-load testing facilities operating under the applicable national HIV-control programme.

Study Duration
The study was conducted for 12 months.

Sample Size
A total of 80 male patients living with HIV were included. The sample size was based on the previously reported prevalence of hypogonadism of approximately 29.4% among men living with HIV, subject to the feasibility of recruitment during the specified study period. Eligible participants were recruited consecutively until the required sample size was achieved.

Inclusion Criteria
1. Male patients aged 18-70 years were included.
2. Patients with a confirmed diagnosis of HIV infection were included, irrespective of their ART status or treatment regimen.
3. Patients attending the outpatient department or admitted to the affiliated hospitals during the study period were considered eligible.
4. Patients who provided written informed consent were included.

Exclusion Criteria
1. Patients who were unwilling or unable to provide written informed consent were excluded.
2. Male patients younger than 18 years or older than 70 years were excluded.
3. Patients with known hypothyroidism, adrenal insufficiency, hyperprolactinaemia, or pituitary disease were excluded because these conditions could independently alter gonadal hormone concentrations.
4. Patients receiving testosterone-replacement therapy, gonadotropins, anabolic steroids, or other medications directly affecting the hypothalamic-pituitary-gonadal axis were excluded.
5. Patients who were critically ill or from whom an adequate blood sample could not be obtained were excluded.

Procedure and Methodology
Approval was obtained from the Institutional Ethics Committee of BMCRI before commencement of the study. Permission was also obtained from the concerned institutional departments and the Karnataka State AIDS Prevention Society, wherever applicable. The purpose and procedures of the study were explained to each eligible participant, and written informed consent was obtained.

Participants were enrolled consecutively according to the eligibility criteria. Information regarding age, occupation, duration of HIV infection, ART status, duration and regimen of ART, adherence to treatment, comorbidities, opportunistic infections, and relevant medication history was recorded using a predesigned study proforma. A general physical and systemic examination was performed. Symptoms suggestive of androgen deficiency, including reduced libido, erectile dysfunction, fatigue, reduced strength, loss of muscle mass, and decreased spontaneous or morning erections, were documented.

Venous blood was collected for the estimation of free testosterone, LH, and FSH. The available HIV viral-load result was verified from the participant's treatment record when it had been performed within the clinically relevant monitoring period. When an eligible recent result was unavailable, a plasma sample was obtained and processed for HIV-1 RNA estimation according to the national programme protocol.

Participants were classified as having normal gonadal function, primary hypogonadism, or secondary hypogonadism according to their testosterone and gonadotropin profiles and the laboratory reference ranges. Primary hypogonadism was identified by reduced testosterone accompanied by elevated LH and/or FSH. Secondary hypogonadism was identified by reduced testosterone accompanied by low or inappropriately normal LH and FSH concentrations. Gonadal hormone concentrations were subsequently compared across viral-load categories, and their correlations with quantitative viral-load values were examined where measurable values were available.

Sample Processing

Blood samples for hormonal assays were collected under aseptic precautions, preferably during the morning hours because testosterone demonstrates diurnal variation. The required quantity of venous blood was collected in an appropriate plain or serum-separator tube. After clot formation, the sample was centrifuged, and the separated serum was analysed for free testosterone, LH, and FSH using the immunoassay method routinely employed by the institutional laboratory. Internal quality-control procedures and the manufacturer-specified reference ranges were followed.

For viral-load estimation, venous blood was collected in an ethylenediaminetetraacetic acid tube. Plasma was separated by centrifugation and tested for HIV-1 RNA using a validated nucleic-acid amplification method. When immediate testing was not possible, plasma was maintained at 2-8°C for a maximum of five days and transported under a maintained cold chain to the designated viral-load laboratory. Viral-load findings were documented as target not detected, below the assay's quantification limit, or as HIV RNA copies/mL, as reported by the testing laboratory.

Data Collection

Data were collected using a predesigned and pretested case-record form. The form contained participant identification codes, sociodemographic characteristics, relevant clinical history, HIV-related details, ART regimen and duration, treatment adherence, comorbid conditions, examination findings, gonadal symptoms, hormone concentrations, and viral-load results. ART and viral-load details were cross-checked with available ART-centre records. Each form was reviewed for completeness before data entry. Participant confidentiality was maintained by using unique study codes rather than names in the analytical database.

Statistical Methods

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 20.0. Quantitative variables were summarised using mean and standard deviation when normally distributed and median with interquartile range when distributions were skewed. Categorical variables were presented as frequencies and percentages.

Normality was evaluated using the Shapiro-Wilk test and graphical methods. Mean hormone concentrations between two viral-load groups were compared using the independent-samples *t* test; the Mann-Whitney *U* test was used for non-normally distributed variables. Comparisons involving more than two groups were performed using one-way analysis of variance or the Kruskal-Wallis test, as appropriate. Associations between categorical variables, including hypogonadal status and viral-load category, were assessed using the chi-square test or Fisher's exact test.

The relationship between quantitative gonadal hormone concentrations and viral load was evaluated using Pearson's or Spearman's correlation coefficient, depending on data distribution. Where appropriate, multivariable logistic regression was used to examine whether detectable or unsuppressed viral load was independently associated with hypogonadism after adjusting for potential confounders such as age, duration of HIV infection, ART duration, ART regimen, and relevant comorbidities. Effect estimates were reported with 95% confidence intervals. All tests were two-tailed, and P<0.05 was considered statistically significant.

Results

Table 1: Association between gonadal hormone levels and HIV viral-load status among male patients living with HIV (N=80)

Gonadal hormone	Viral load more than TND (n=8), Mean (SD)	Viral load TND (n=72), Mean (SD)	Mean difference (95% CI)	Test of significance	P value
Free testosterone, pg/mL	6.39 (3.66)	7.75 (4.57)	-1.36 (-4.50 to 1.78)	Welch's t=-0.97	0.356
FSH, mIU/mL	4.37 (2.87)	6.13 (5.42)	-1.75 (-4.33 to 0.83)	Welch's t=-1.46	0.167
LH, mIU/mL	3.03 (2.85)	4.77 (2.98)	-1.74 (-4.16 to 0.68)	Welch's t=-1.63	0.138

The mean serum free testosterone level was lower among participants with viral load more than TND than among those with TND viral load [6.39 (3.66) versus 7.75 (4.57) pg/mL]. The mean difference was -1.36 pg/mL (95% CI: -4.50 to 1.78); however, this difference was not statistically significant (Welch's t=-0.97, P=0.356). Similarly, participants with viral load more than TND had lower mean FSH [4.37 (2.87) versus 6.13 (5.42) mIU/mL; MD=-1.75, 95% CI: -4.33 to 0.83; P=0.167] and LH levels [3.03 (2.85) versus 4.77 (2.98) mIU/mL; MD=-1.74, 95% CI: -4.16 to 0.68; P=0.138].

Table 2: Serum gonadal hormone levels according to hypogonadal status among male patients living with HIV (N=80)

Hormone	Total (N=80), Mean (SD); 95% CI	Eugonadism (n=49), Mean (SD)	Primary hypogonadism (n=23), Mean (SD)	Secondary hypogonadism (n=8), Mean (SD)	Test of significance	P value
Free testosterone, pg/mL	7.62 (4.49); 6.62-8.62	10.25 (3.68)	3.37 (1.41)	3.71 (1.76)	One-way ANOVA F=47.18	<0.001*
FSH, mIU/mL	5.95 (5.23); 4.79-7.11	5.39 (4.55)	8.09 (6.68)	3.24 (0.93)	One-way ANOVA F=3.49	0.035*
LH, mIU/mL	4.59 (3.00); 3.92-5.26	4.91 (3.21)	4.60 (2.72)	2.63 (1.50)	One-way ANOVA F=2.04	0.136

Statistically significant at P<0.05.

Among the 80 participants, the overall mean free testosterone level was 7.62 (4.49) pg/mL (95% CI: 6.62-8.62). Participants with eugonadism had a substantially higher mean free testosterone level [10.25 (3.68) pg/mL] than those with primary [3.37 (1.41) pg/mL] or secondary hypogonadism [3.71 (1.76) pg/mL]. The difference across the three groups was statistically significant (F=47.18, P<0.001). The overall mean FSH level was 5.95 (5.23) mIU/mL (95% CI: 4.79-7.11), with the highest level observed in primary hypogonadism [8.09 (6.68) mIU/mL], followed by eugonadism [5.39 (4.55) mIU/mL] and secondary hypogonadism [3.24 (0.93) mIU/mL]. This difference was also statistically significant (F=3.49, P=0.035). The overall mean LH level was 4.59 (3.00) mIU/mL (95% CI: 3.92-5.26). Although LH was lowest in the secondary hypogonadism group [2.63 (1.50) mIU/mL], its variation across the three groups was not statistically significant (F=2.04, P=0.136).

Table 3: HIV viral-load status of the study participants (N=80)

HIV viral-load status	n (%)	95% CI for proportion	Test of significance†	P value
Target not detected (TND)	72 (90.0)	81.5%-94.8%	z=7.16	<0.001*
More than TND/detectable	8 (10.0)	5.2%-18.5%	z=-7.16	<0.001*
Total	80 (100.0)	-	-	-

†One-sample proportion z-test against a reference proportion of 50%.
Statistically significant at P<0.05.

Of the 80 male patients living with HIV, 72 (90.0%; 95% CI: 81.5%-94.8%) had a target-not-detected viral load, whereas only 8 (10.0%; 95% CI: 5.2%-18.5%) had a detectable viral load. The proportion of participants with TND viral load was significantly greater than the reference

proportion of 50% (z=7.16, P<0.001). Conversely, the proportion with detectable viral load was significantly below 50% (z=-7.16, P<0.001). These findings indicate that most participants had achieved virological suppression or had circulating HIV RNA below the assay's detection threshold.

Table 4: Association between hypogonadal status and HIV viral-load status among male patients living with HIV (N=80)

HIV viral-load status	Eugonadism, n (%)	Primary hypogonadism, n (%)	Secondary hypogonadism, n (%)	Any hypogonadism, n (%)	Effect estimate for any hypogonadism (95% CI)	Test of significance	P value
More than TND (n=8)	5 (62.5)	1 (12.5)	2 (25.0)	3 (37.5)	OR=0.94 (0.21-4.26)	Pearson χ^2=2.82, df=2†	0.244
TND (n=72)	44 (61.1)	22 (30.6)	6 (8.3)	28 (38.9)	Reference	-	-
Total (N=80)	49 (61.3)	23 (28.8)	8 (10.0)	31 (38.8)	-		

Among the eight participants with viral load more than TND, 5 (62.5%) had eugonadism, 1 (12.5%) had primary hypogonadism, and 2 (25.0%) had secondary hypogonadism. Any form of hypogonadism was therefore present in 3 (37.5%) participants in this group. Among the 72 participants with TND viral load, 44 (61.1%) had eugonadism, 22 (30.6%) had primary hypogonadism, and 6 (8.3%) had secondary hypogonadism, giving an overall hypogonadism prevalence of 38.9%. The odds of any hypogonadism were comparable between participants with viral load more than TND and those with TND viral load (OR=0.94, 95% CI: 0.21–4.26). The distribution of gonadal status did not differ significantly according to viral-load status (Pearson χ^2=2.82, df=2, P=0.244).

Discussion

Association between gonadal hormone levels and HIV viral-load status

In the present study, mean free testosterone, FSH and LH levels were lower among patients with viral load more than target not detected (TND) than among those with TND viral load. However, none of these differences reached statistical significance. Free testosterone was 6.39±3.66 pg/mL in patients with detectable viral load compared with 7.75±4.57 pg/mL in those with TND viral load (P=0.356). Similarly, the differences in FSH (4.37±2.87 vs 6.13±5.42 mIU/mL; P=0.167) and LH (3.03±2.85 vs 4.77±2.98 mIU/mL; P=0.138) were not significant. The consistently lower hormone concentrations in the detectable viral-load group may indicate a possible biological trend, but the wide confidence intervals and the small number of participants with detectable viral load limited statistical precision.

These findings are consistent with Gomes et al. (2016) [3], who evaluated 245 men receiving combined ART and found no significant association of testosterone deficiency with viral count or viral suppression. In their study, 82.4% of participants had viral load below 50 copies/mL, and viral suppression was observed in 76.7% of men with testosterone deficiency and 84.5% of those without testosterone deficiency (P=0.255). This supports the present finding that testosterone deficiency may persist even when HIV replication is adequately suppressed.

Rochira et al. (2015) [1] reported that low testosterone in men living with HIV was more strongly associated with poor general health, multimorbidity and frailty than with an isolated HIV-related marker. Similarly, Kietsiriroje (2015)[2] described hypogonadism in HIV as a multifactorial disorder involving chronic illness, nutritional status, opportunistic infections, medications and alterations throughout the hypothalamic-pituitary-gonadal axis. Wong et al. (2017)[5] and Mirza et al. (2018)[7] also emphasised that viral replication alone cannot explain gonadal dysfunction in treated HIV infection because age, obesity, chronic inflammation, liver disease, medications, substance use and altered sex hormone-binding globulin (SHBG) may independently affect testosterone levels.

Nevertheless, the absence of a significant association in the present cross-sectional analysis does not exclude a longitudinal effect of HIV disease activity. Iddi et al. (2025)[15] observed significant increases in testosterone and LH after six and 12 months of ART initiation. Approximately half of the men with baseline hypogonadism achieved normal testosterone levels within one year, and testosterone change was significantly associated with initial viral load (P=0.049). Their longitudinal findings suggest that reduction in viral replication and improvement in general health following ART may facilitate recovery of the hypothalamic-pituitary-gonadal axis. The difference from the present results could be explained by the predominance of virally suppressed, ART-treated participants in the current study and the inclusion of only eight men with detectable viral load.

Gonadal hormone levels according to hypogonadal status

The overall mean free testosterone level was 7.62±4.49 pg/mL. As expected from the biochemical definition of hypogonadism, free testosterone differed markedly across the gonadal-status categories: 10.25±3.68 pg/mL in eugonadal men, 3.37±1.41 pg/mL in primary hypogonadism and 3.71±1.76 pg/mL in secondary hypogonadism (P<0.001). FSH was highest in primary hypogonadism (8.09±6.68 mIU/mL) and lowest in secondary hypogonadism (3.24±0.93 mIU/mL), with a significant overall group difference (P=0.035). This pattern was physiologically plausible because impaired testicular function reduces gonadal negative feedback and results in increased pituitary gonadotropin secretion. Conversely, central or functional suppression of the hypothalamic-pituitary axis produces low testosterone with low or inappropriately normal gonadotropins.

The mean LH concentration was lower in secondary hypogonadism than in the other two groups, but the overall difference was not statistically significant (P=0.136). This may reflect the pulsatile nature of LH secretion, within-person variation, relatively small secondary-hypogonadism group and use of a single hormone measurement. Bhasin et al. (2018) [8] recommended diagnosing androgen deficiency only in men with compatible clinical features and consistently low morning testosterone concentrations, with repeat testing and additional LH and FSH measurement to distinguish primary from secondary hypogonadism.

Gomes et al. (2016) [3] reported testosterone deficiency in 29.4% of men receiving ART; 56.9% had hypogonadotropic dysfunction and 43.1% had hypergonadotropic dysfunction. Their findings demonstrated that both primary and secondary forms occur among men living with HIV. In contrast, the present study showed a larger primary-hypogonadism component, with primary hypogonadism in 28.8% and secondary hypogonadism in 10.0% of the complete sample. Differences in patient age, ART exposure, disease severity, laboratory methods, reference ranges and exclusion of other endocrine disorders may have contributed to the contrasting distributions.

Pongener et al. (2019) [9] found hypogonadism in 23.3% of ART-treated HIV-positive men in northeastern India, of whom approximately 85.7% had secondary hypogonadism. Coelho Gomes et al. (2017) [6] also described severe hypogonadotropic hypogonadism in men with HIV despite normal imaging and relatively preserved immune status. These studies indicate that functional or central suppression is often prominent in HIV-associated hypogonadism. However, the higher FSH concentration in the primary-hypogonadism group in the present study suggests that direct or acquired testicular dysfunction also made an important contribution.

The observed prevalence and hormone pattern must also be interpreted in relation to the method used to assess androgen status. Lachâtre et al. (2017) [4] reported hypogonadism in 12.4% of young and middle-aged men receiving effective ART when a reliable free-testosterone assessment was used. De Vincentis et al. (2022) [14] demonstrated that the prevalence of biochemical hypogonadism varied according to

whether sex steroids were measured using chemiluminescent immunoassay or liquid chromatography-tandem mass spectrometry. They found a prevalence of 17.1% when overt and compensated hypogonadism were classified using calculated free testosterone, gonadotropins and SHBG.

Pezzaioli et al. (2021) [13] further demonstrated the importance of SHBG and calculated free testosterone in symptomatic men with HIV. HIV infection and certain ART regimens may increase SHBG, producing apparently normal total testosterone despite reduced biologically available testosterone. Therefore, the use of free testosterone in the present study was appropriate, although simultaneous measurement of total testosterone, SHBG and albumin and confirmation with a second morning sample would have provided a more complete evaluation.

HIV viral-load status

Viral load was target not detected in 72 (90.0%) participants, whereas only 8 (10.0%) had detectable viral load. This high TND proportion indicates effective virological control in most participants and is consistent with successful engagement in ART services. It also explains the limited ability of the study to identify differences in gonadal hormones according to viral-load status because the detectable group was comparatively small.

The viral-suppression proportion was higher than the 82.4% reported by Gomes et al. (2016) [3] in an ART-treated cohort. Lachâtre et al. (2017) [4] similarly evaluated young and middle-aged men on effective ART and showed that hypogonadism remained more common than in the general population despite virological control. Thus, successful viral suppression does not necessarily normalise gonadal function. Persistent immune activation, ageing, altered body composition, ART duration and non-communicable comorbidities may continue to influence testosterone production after viral suppression has been achieved.

Santi et al. (2021) [11], in a meta-analysis, estimated an overall hypogonadism prevalence of approximately 26% among men living with HIV and found that prevalence estimates were higher when free rather than total testosterone was used. Maffezzoni et al. (2020) [10] similarly reported that hypogonadism remains clinically important among men with HIV in the ART era, even among populations with effective treatment. These observations support the interpretation that viral suppression and gonadal recovery represent related but distinct clinical outcomes.

Association between hypogonadal status and viral load

Any hypogonadism was present in 37.5% of participants with viral load more than TND and 38.9% of those with TND viral load. The corresponding odds ratio was 0.94 (95% CI: 0.21-4.26), indicating almost identical odds of hypogonadism in the two viral-load groups. The distribution of eugonadism, primary hypogonadism and secondary hypogonadism also did not differ significantly by viral-load status (P=0.244). The wide confidence interval indicates considerable uncertainty, particularly because only eight participants had detectable viral load.

This finding agrees with Gomes et al. (2016) [3], who found no significant difference in viral suppression according to testosterone-deficiency status. De Vincentis et al. (2021) [12] proposed that hypogonadism in contemporary HIV care is often functional and more closely related to overall health, body composition and comorbidities than to a single measure of virological activity. Postel et al. (2021) [12] also found functional hypogonadism and testosterone deficiency to be more frequent among ageing men with HIV than among HIV-negative men, highlighting the importance of age-related and metabolic determinants.

The hypogonadism prevalence of 38.8% in the present study was higher than that reported by Lachâtre et al. (2017) [4], Pongener et al. (2019) [9], Maffezzoni et al. (2020) [10] and the meta-analysis by Santi et al. (2021) [11], but it remained within the 13%-40% range described in contemporary reviews. Possible explanations include differences in free-testosterone thresholds, participant selection, timing of sample collection, prevalence of clinical symptoms, ART regimens and the absence of repeat hormone confirmation.

Conclusion

Gonadal dysfunction was common among male patients living with HIV, with hypogonadism identified in 38.8% of participants. Free testosterone differed significantly among eugonadal, primary-hypogonadal and secondary-hypogonadal groups, while FSH also demonstrated a significant overall difference. However, free testosterone, FSH and LH levels did not differ significantly between participants with detectable and target-not-detected viral loads. Hypogonadal status was also not significantly associated with viral-load status. These findings suggest that gonadal dysfunction in men living with HIV is multifactorial and may persist despite virological suppression. Assessment of gonadal function should therefore be based on clinical symptoms and comprehensive hormonal evaluation rather than viral-load status alone.

LIMITATIONS OF STUDY

This study had several limitations. Its cross-sectional design prevented determination of temporal or causal relationships between viral load and gonadal hormone abnormalities. The relatively small sample size, particularly the inclusion of only eight participants with detectable viral load, reduced statistical power and resulted in wide confidence intervals. The study was conducted at a single tertiary-care centre, which may limit generalisability. Hormonal assessment was based on a single measurement; repeat morning testing was not performed to confirm testosterone deficiency or account for biological and diurnal variation. Total testosterone, SHBG, albumin and estradiol were not comprehensively evaluated, limiting assessment of calculated free testosterone and compensated hypogonadism. Potential confounders such as age, BMI, ART regimen and duration, treatment adherence, CD4 count, duration of HIV infection, nutritional status, smoking, alcohol use and comorbidities were not fully controlled through multivariable analysis. Categorisation of viral load as TND or detectable also prevented evaluation of a dose-response relationship between quantitative HIV RNA levels and gonadal hormones.

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