

Original Research Article

A Study of Gonadal Hormones in HIV Seropositive Subjects Attending the ART Center at K.R. Hospital, a Tertiary Care Hospital in Mysuru

Abstract:

Aims: HIV infection and AIDS remain global health challenges, with many individuals suffering from endocrine disorders such as gonadal dysfunction. This study assesses the levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estradiol in HIV-positive individuals before and after six months of antiretroviral therapy (ART).

Study Design: Clinical observational study.

Place and Duration of Study: ART Center, K.R. Hospital, Mysuru.

Methodology: The clinical–observational study involved seventy subjects who were HIV positive, who were recruiting to ART clinic which is located at KR hospital Mysuru. The subjects were split into two groups according to their CD4 count (≤ 200 cells/ μ L ND >200 cells/ μ L). The baseline values were measured for LH, FSH, testosterone and estradiol just prior to ART and the levels of hormones were measured again six months after commencing ART.

Results: Our study conducted among 70 subjects, 38 were males and 32 were females, average age being around 40 years. These subjects were divided into two groups based on CD4 counts (≤ 200 cells/ μ L and >200 cells/ μ L). Gonadal hormone level were checked pre-ART and six months post-ART therapy. After six months of ART therapy, there was significant improvement in testosterone (7.93 pg/mL to 8.94 pg/mL ($p < 0.0001$)) and LH level noted among male subjects, estradiol and FSH levels were not improved significantly. Same degree of improvement in hormone level were not seen in female subjects. Hypogonadism improved from 18.57% improved to 69.23% after six-month post-ART therapy. This signifies role of ART therapy in improvement in gonadal dysfunction.

Conclusion: Gonadal deficiency or more specifically hypogonadism is common among patients infected with HIV. The improvement in male testosterone and LH levels after ART suggests that hypogonadism may reverse in some cases. However, these observations need long term and larger volume studies to support the hypothesis.

Key words: Gonadal Hormones, ART therapy, HIV, Hypogonadism

1. INTRODUCTION:

While ART has led to significantly improved longevity and outcomes in HIV infection, it is not the silver bullet that eradicates the risk that the pathogen and its advanced form - AIDS present

to the society¹. Although the removal of AIDS as a ‘terminal disease’ is a significant step forward for society and shifts the focus towards better management of the disease, research indications show the shift with increasing longevity has also highlighted attention towards multiple comorbidities including gonadal disorders.

People with HIV AIDS do present with a variety of endocrine disorders, but perhaps one of the most prominent is Gonadal dysfunction most notably hypogonadism². This condition is defined as having low sex hormones testosterone in men, and estradiol in women, and having this condition can lead to loss of interest in sexual activities and infertility in individuals. For HIV patients, this disorder has been shown to postpone the development of the disease as well as to impair the immune system³. According to studies, as many as half of men with advanced stages of HIV may actually have a secondary and primary degenerative disorder. People with primary gonadal failure experience one of the more common problems of secondary hypogonadism which is associated with hypothalamic-pituitary-gonadal HPG axis.

While ART has been effective at restoring immune function and reducing viral load in patients, little investigation to date has evaluated overall endocrine function of HIV patients on ART being the gonadal hormones. Existing studies suggest improved ART hormone levels in hypogonadism, but overall results are conflicting. This study aims to investigate the effect of ART on gonadal function by studying the serum levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone, and estradiol among HIV-positive individuals on ART for six months.

2.METHODOLOGY

2.1 Study Design and Participants

This observational study was conducted at the ART Center, K.R. Hospital, Mysuru. For the level of significance of 5% and allowable error of 10%, using estimation set up technique the sample size is estimated as 70. A P value of <0.05 was considered as statistically significant. A total of 70 HIV-positive patients were included and divided in two groups on the basis of CD4 cell count. Patients in groups A and B had CD4 count ≤ 200 and >200 cell/ μ L, respectively. Baseline hormone level was measured before the start of ART, and the patients were followed up for 6 months and the hormone levels were measured again.

2.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

- HIV-positive subjects aged ≥ 18 years providing informed consent.

Exclusion Criteria:

1. Hormonal treatment within six months.
2. Congenital gonadal disorders.
3. Renal or liver failure.
4. Pregnancy.

2.3 Data Collection and Analysis

Baseline hormone levels were measured before ART initiation and after six months. Statistical analysis was performed using SPSS, with $p < 0.05$ considered significant.

3. RESULTS:

A cross-sectional study of 70 HIV seropositive patients (38 and 54.28% male and 32 and 45.71%) have been undertaken to correlate hormonal changes along with CD4 counts in ART patients from a tertiary care center. CD4 counts ($<200/\mu\text{L}$ and $>200/\mu\text{L}$) were used for stratum and participants (primarily of 20–40 years age group; mean = 40.25 years) were tracked for six months. At baseline 18.57% were hypogonadal (23.09% males and 10.19% females). After 6 months on ART, 69.23% of subjects with hypogonadism no longer qualified ($P < .05$), as shown in Table 1 and Figure 1.

Category	Total Subjects	Subjects with Hypogonadism	Percentage with Hypogonadism (%)	Improved after ART	Percentage Improved (%)
Overall	70	13	18.57	9	69.23
Males	38	9	23.09	6	66.67
Females	32	4	10.19	3	75

Table 1: Highlights the prevalence of hypogonadism among seropositive subjects and showing improvement post ART therapy.

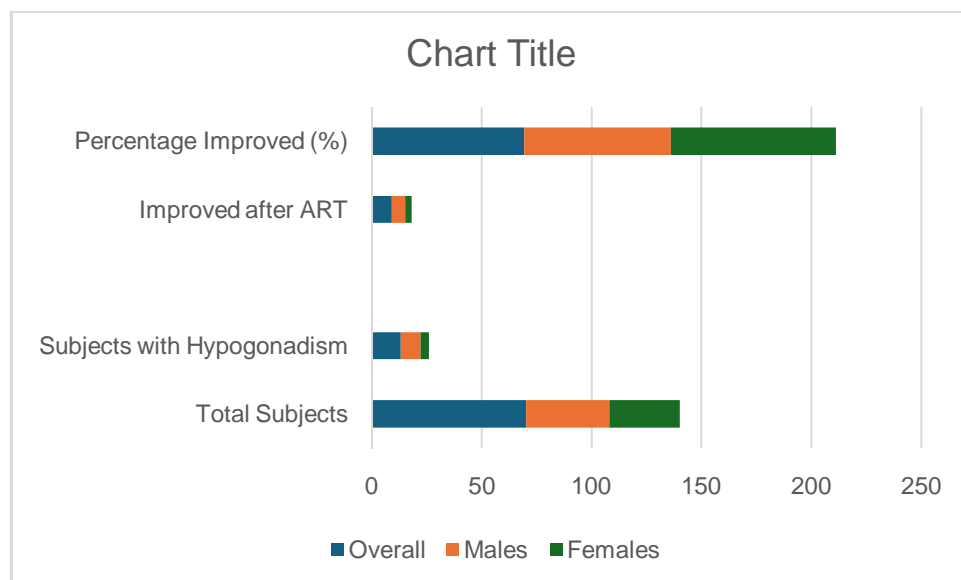


Figure 1: A total of 70 subjects were studied, among whom 13 (9 males and 4 females) had hypogonadism. Of these, 9 subjects showed improvement after six months of ART therapy

The increase in CD4 count after ART initiation was statistically significant ($p = 0.034$), as shown in Table 2, where average baseline CD4 estimate of $168.05/\mu\text{L}$ increased to $181.19/\mu\text{L}$. Changes in hormonal level post-ART therapy were different among male and females. Improvement in hypogonadal state were more significant in subjects with lower CD4 counts (ie $<200/\mu\text{L}$), as can be seen in Figure 2. Among male subjects, testosterone levels improved significantly from 7.93 to 8.94 pg/mL ($p < 0.0001$), as can be seen in Figure 3. Results also showed improvement in LH and FSH levels from 8.45 to 9.20 mIU/mL , $p < 0.0001$ and from 8.32 to 9.35 mIU/mL , $p < 0.0001$, respectively. Among females there were no significant improvement in hormonal levels. Testosterone levels improved from 2.88 to 3.87 pg/mL ($p = 0.00023$) and estradiol levels improved from 61.41 to 66.92 pg/mL ($p = 0.00032$).

	Pre ART	Post ART	p valve
CD4 counts	168.05	181.19	0.034

Table 2: Shows improvement in CD4 counts after 6 months of ART therapy.

Hormone	Pre-ART Levels (Mean \pm SD)	Post-ART Levels (Mean \pm SD)	p-Value
Testosterone (pg/mL)	7.93 ± 2.18	8.94 ± 2.78	<0.0001
Luteinizing Hormone (LH, mIU/mL)	$8.45 \pm$	$9.20 \pm$	<0.0001

	1.56	1.83	
Follicle-Stimulating Hormone (FSH, mIU/mL)	8.32 ± 1.73	9.35 ± 2.01	<0.0001

Table 3: Reveals hormonal levels pre-ART and six months post-ART, with significant improvement after 6 months of ART therapy in seropositive men subjects

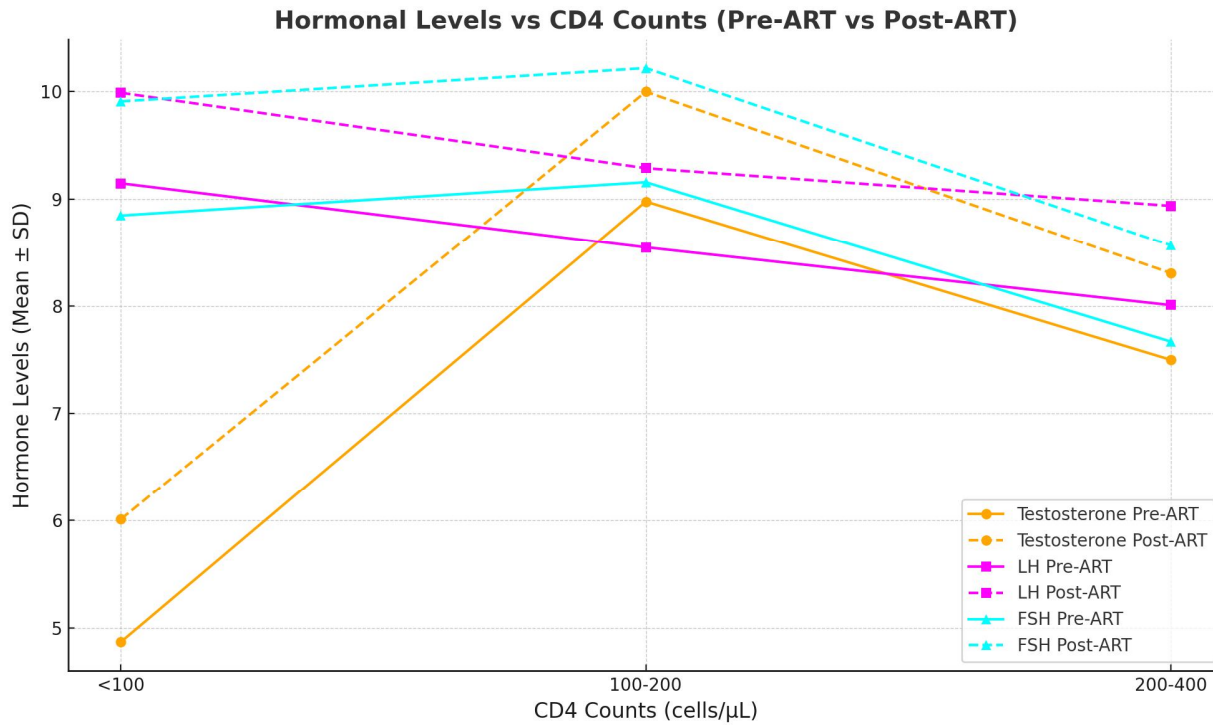


Figure 2: Graph shows hormone levels (Testosterone, LH,FSH) with CD4 counts, pre-ART and post-ART therapy.

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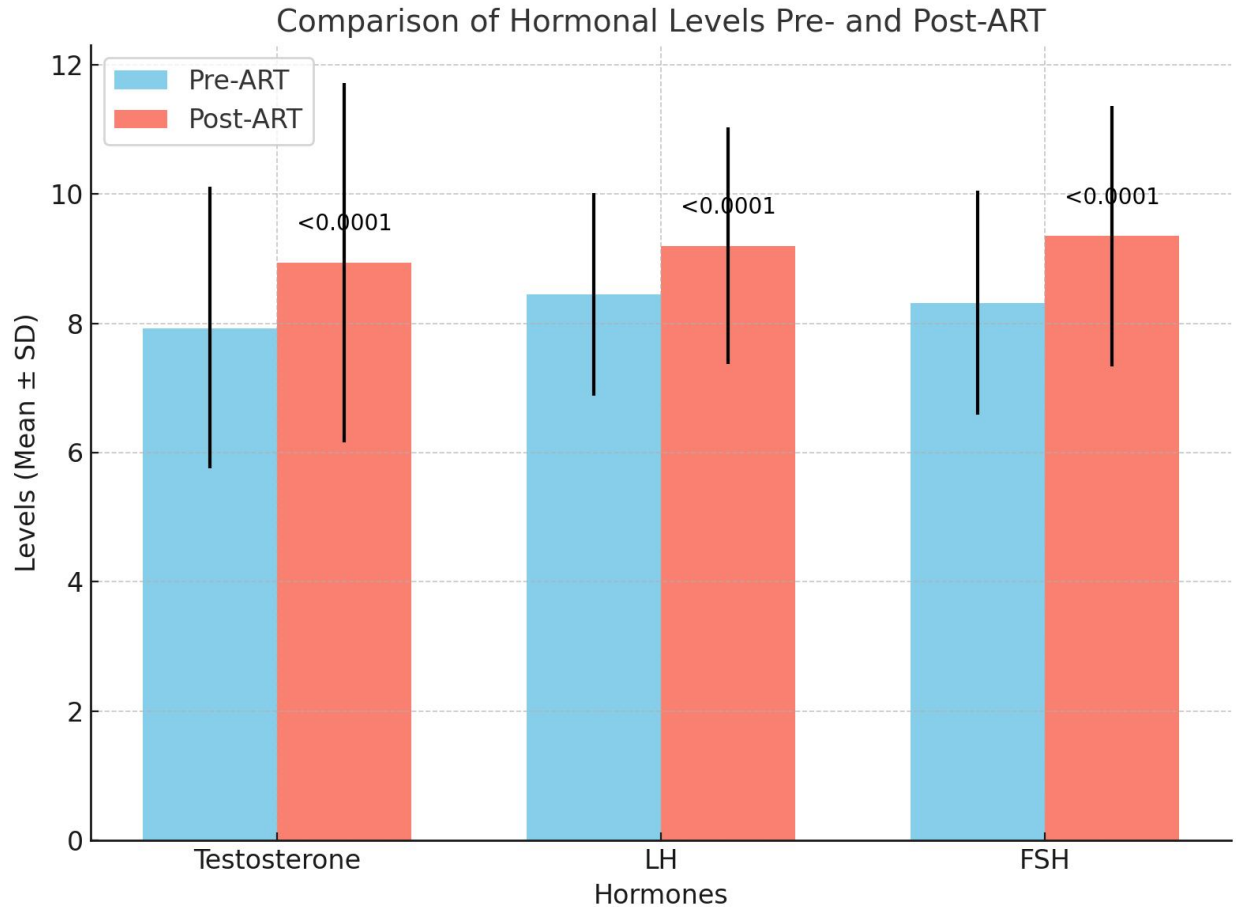


Figure 3: This bar chart illustrates mean values (+/- SD) of Testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) pre and post six months of ART therapy, with significant improvement post six months of ART therapy.

4. DISCUSSION:

Hypogonadism is a very common endocrine disorder which is prevalent in HIV infected individuals, which was validated in our study. Hypogonadism, crude for low serum testosterone in men and low estradiol in women, has increased morbidity, losing libido, infertility, muscular atrophy and fatigue. The prevalence of hypogonadism in our study (18.57%) is comparable to those reported in a previous study conducted in a setting of high prevalence of hypogonadism (20%–50%) in HIV positive males of late stages⁴⁻⁶.

Our data demonstrate that what seems to be an effective method for increasing testosterone levels in male patients is the use of ART for six months (7.93 pg/mL before ART and 8.94 pg/mL with ART; $p < 0.0001$). This finding might indicate that ART may play a role in

amelioration of hypogonadism and thereby improve the quality of life of such patients. Concomitant increases in levels of LH and FSH were reported indicating that some rescue of the functions of the hypothalamic-pituitary-gonadal HPG axis was likely obtained along with testosterone levels. Moreover, the 8fold increase in LH and FSH levels ($p < 0.0001$) also confirms that conclusion.

Similar to male patients, female patients did not show significant improvement in testosterone and estradiol levels post ART, rather had only mild differences of testosterone and estradiol. Mean testosterone level in women, however, did increase (2.88 pg/mL vs. 2.98 pg/mL, $p = 0.00023$) as did estradiol (61.41 pg/mL vs. 66.92 pg/mL, $p = 0.00032$) but the effect on therapy is uncertain. This may be due to the relatively small number of female patients or perhaps lower gonadal dysfunction in women compared with men. The gender differences in the effects of ART may also mimic the gender differences in gonadal loss responses of persons with HIV.

The pathophysiology of hypogonadism in HIV-infected patients is complex and likely includes multisystem mechanisms. Alternatively, the direct impact of the HIV virus on the HPG axis, which results in reduced gonadotropin (LH and FSH) secretion and diminished testosterone or estradiol may also be considered⁷. Handsome, they may also arise from opportunistic infections and malignancies (eg., Kaposi's sarcoma and cytomegalovirus) impacting on gonadal tissues or the hypothalamic-pituitary region. Leydig cell dysfunction and inhibitory steroidogenesis have also been associated with chronic inflammation and higher pro-inflammatory cytokines (e.g., interleukin-1, tumor necrosis factor-alpha).

Interestingly, in contrast with previous reports the majority cases of hypogonadism identified in this study were secondary with very few being primary^{8,9}. Secondary Hypogonadism: low or normal FSH/LH; low sex hormones; usually a pituitary/hypothalamus issue. In our cohort, this effect was likely mediated primarily through the effects of chronic HIV infection, with added contributions from potential CNS involvement with opportunistic infections or malignancies.

Our findings on the influence of ART on gonadal function contribute to the published literature that indicates that ART is beneficial for the resolution of certain endocrine derangements in HIV-infected patients. Although the exact mechanism of ART-induced gonadal hormone elevation is not fully illuminated, improved immune restoration and reduced chronic immune activation in successfully ART may be an important prerequisite. ART might also affect gonadal function indirectly, through modification of HPG axis integrity and mitigation of chronic disease-related systemic sequelae through decreased viral load and decreasing the risk of opportunistic infections.

5.CONCLUSION:

Gonadal dysfunction, especially hypogonadism, is common in patients with HIV and is linked to considerable morbidity. The results demonstrated that ART improves gonadal hormones, especially doing so in males, which indicates its possible therapeutical role in approach of hypogonadism in this population. Further longitudinal studies are needed to elucidate these

findings and understand the long-term effects of ART on endocrine function in individuals with HIV.

6.LIMITATIONS:

Although our study provides some insight, there are a number of limitations. The study had relatively small sample size which means, it might not be able to represent the general public. Moreover if six months might have been insufficient to describe ART impact on endocrine function. An additional limitation is the inability to directly assess patient adherence to ART, as compliance can affect hormone levels. Larger cohorts and extended follow-up in future studies will provide better insight regarding long-term effects of ART on gonadal dysfunction.

ETHICAL APPROVAL

Ethical approval was obtained from Mysore Medical College and Research Institute, adhering to the Declaration of Helsinki guidelines.

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