Original Research Article

Gonadal Hormonal Changes in HIV-Positive Individuals Following Anti –retroviral Theraphy at K.R. Hospital, 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 patients who were HIV positive, who were recruiting to ART clinic which is located at KR hospital Mysuru. The patientswere split into two groups according to their CD4 count (≤200 cells/μL ND >200 cells/μL). 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 patients,38 were males and 32 were females, average age being around 40 years. These patients were divided into two groups based on CD4 counts (≤200 cells/μL and >200 cells/μL). 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 patients, estradiol and FSH levels were not improved significantly. Same degree of improvement in hormone level were not seen in female patients. 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 society[1]. 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 hypogonadism [2]. 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 system[3]. 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.

Although ART has restored immune function and reduced viral load, there has been limited investigation into its effects on endocrine function, specifically 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.

By providing clarity on these interactions, this study holds significant potential to advance scientific understanding and fill critical gaps in current knowledge. Insights gained from this research could enhance the clinical management of hypogonadism in HIV patients, improve patient outcomes by mitigating related morbidities, and contribute to the broader understanding of how ART impacts overall endocrine health in this population. These findings have the potential to influence future therapeutic strategies and improve the quality of life for individuals living with HIV

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 if estimated as 70. A P value of <0.05 was considered at 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/μL, 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 patientsaged ≥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/µL and >200/µL) 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 patientswith hypogonadism no longer qualified (P <. 05), as shown in Table 1 and Figure 1.

Category	Total Patients	Patientswith 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 patients and showing improvement post ART therapy.

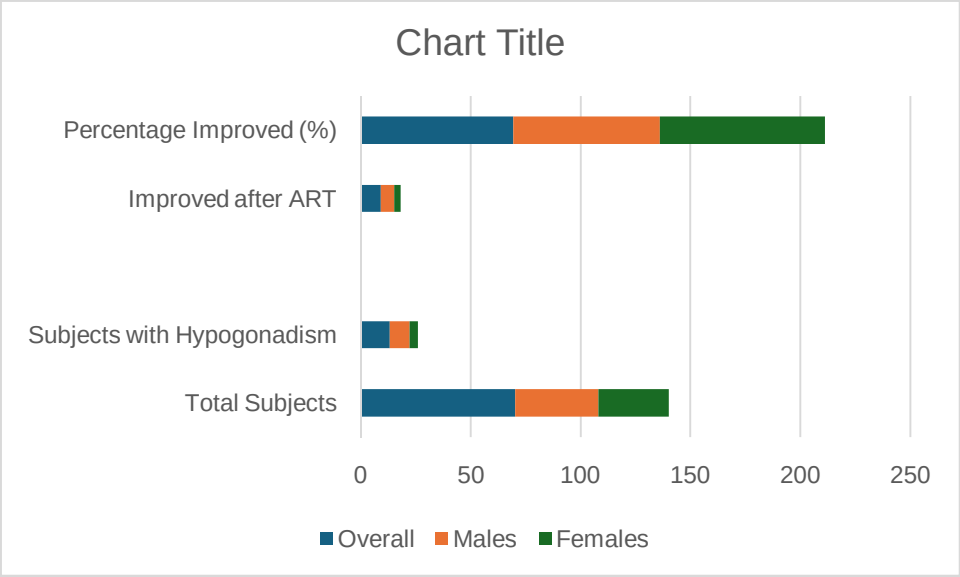

Figure 1: A total of 70 patients were studied, among whom 13 (9 males and 4 females) had hypogonadism. Of these, 9 patients showed improvement after six months of ART therapy

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/µL increased to 181.19/ µL. Changes in hormonal level post-ART therapy were different among male and females. Improvement in hypogonadal state were more significant in patients with lower CD4 counts (ie<200/µL), as can be seen in Figure 2. Among male patients,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 ± SD)	Post-ART Levels (Mean ± SD)	p-Value
Testosterone (pg/mL)	7.93 ± 2.18	8.94 ± 2.78	<0.0001
Luteinizing Hormone (LH, mIU/mL)	8.45 ±	9.20 ±	<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 patients

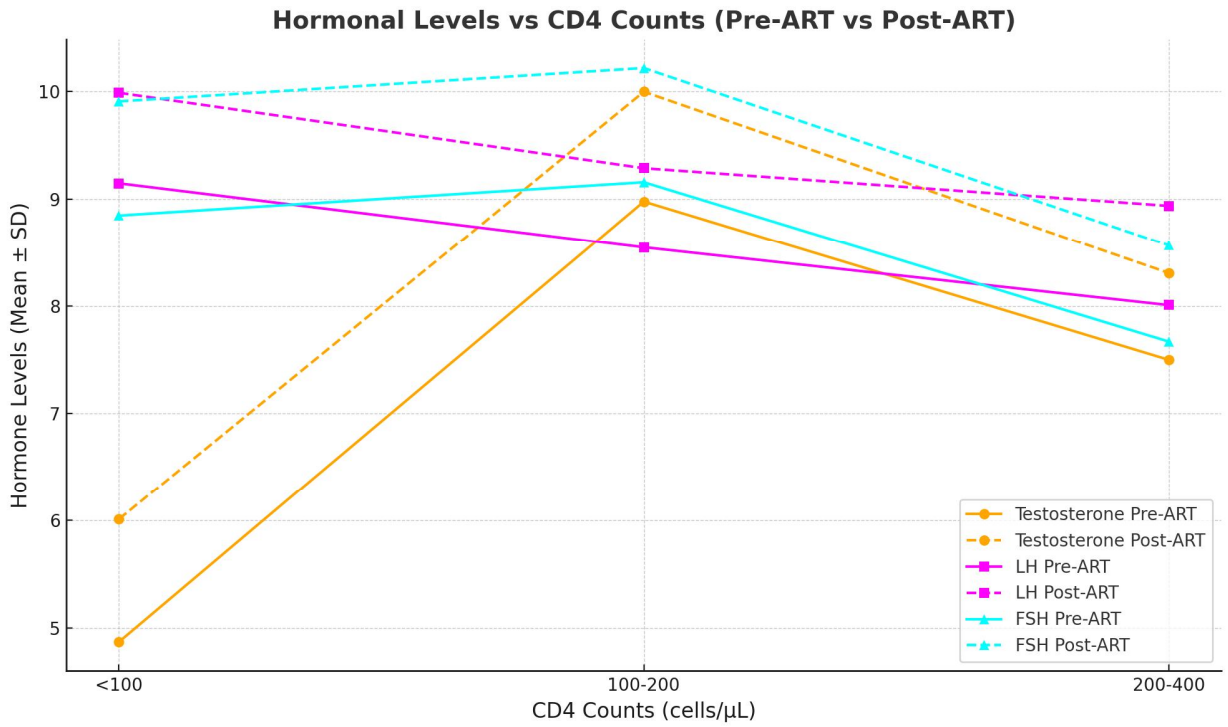

Figure 2: Graph shows hormone levels (Testosterone, LH,FSH) with CD4 counts, pre-ART and post-ART therapy.

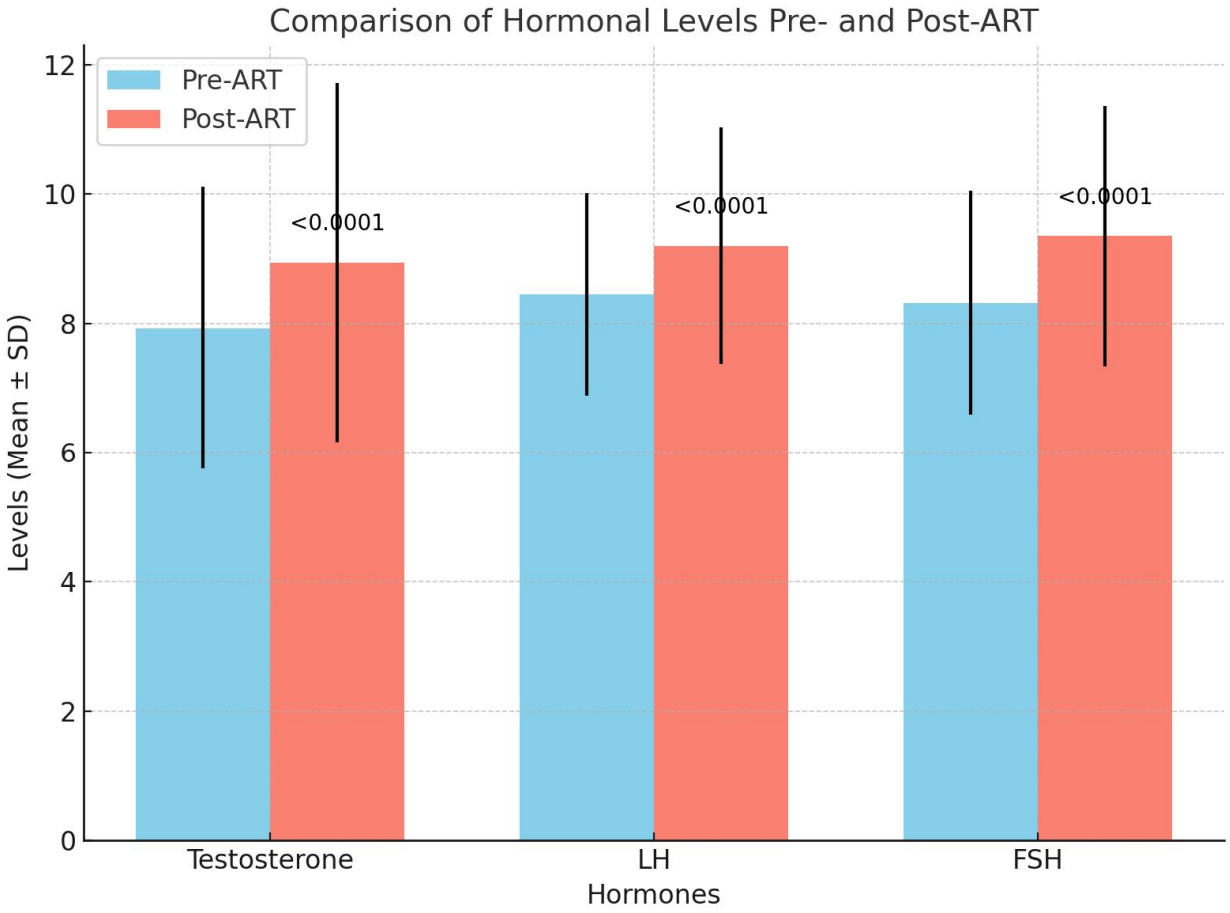

Figure 3: This bar chart illustrations mean values (+/- SD) of Testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) pre and post six months of ART therapy, with significant improvement post six months of ART therapy.

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 stages[4–6].

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, they 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. The lack of significant improvement in females underscores gender-specific physiological differences, warranting further research to explore these disparities. These findings highlight that hormonal responses to ART may not be uniform across sexes, reflecting distinct biological mechanisms[7]. For instance, factors such as differences in baseline hormone levels, gonadal reserve, or immune responses may modulate the effectiveness of ART on endocrine restoration. Exploring these differences in depth could lead to a better understanding of how ART can be optimized for women, ensuring equitable improvements in quality of life.

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[8], which results in reduced gonadotropin (LH and FSH) secretion and diminished testosterone or estradiol may also be considered[9]. Moreover, chronic inflammation driven by HIV and its interplay with sex-specific immune pathways might provide a unique perspective on how gonadal function is affected differently in men and women. This opens new avenues for translational research into gender-sensitive therapeutic strategies[10]. They may also arise from opportunistic infections and malignancies (eg, Kaposi's sarcoma[11] 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[12,13]. 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.Future studies must focus on unraveling the intricate interplay between ART, chronic immune activation, and endocrine function, particularly within the framework of gender-specific

responses. Addressing these gaps could pave the way for precision medicine approaches tailored to the needs of male and female HIV patients alike.

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. Another significant limitation is the inability to directly assess patient adherence to ART, which is a critical factor influencing hormonal outcomes. Non-adherence to ART can lead to suboptimal suppression of viral load, continued immune dysfunction, and persistent gonadal hormone abnormalities. This limitation is particularly important, as variations in adherence could contribute to the observed differences in hormonal response between male and female participants or across CD4 strata. Future studies should incorporate adherence monitoring methods, such as pharmacy refill records or direct measurement of ART plasma levels, to better understand its influence on endocrine recovery.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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