

Original Research Article

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## Role of Hormonal Effects in Men and Women HIV Patients

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### ABSTRACT

#### Keywords

Males and Females (pre-menopausal), Age matched controls, Infected HIV patients, HPA

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The hormones are related to body composition may play an important role male and female in infected HIV patients. We were using both male and female (Beck Depression Inventory Questionnaire). In the current study, we assessed the Endocrine system, the Hypothalamus and Pituitary it can be challenging to problems in people with HIV because certain symptoms may be associated with altered levels of more than one hormone. Such subtle imbalances may have a major impact on quality of life, and there are so many people many benefit from testing of hormone levels and supplementation with HIV patients.

### Introduction

The endogenous glucocorticoids are important in regulating inflammation. Hypothalamic pituitary adrenal axis (HPA) contributes to regulation of T cell activation in HIV. It is an important pathway through which psychological states and HPA axis influence progression of HIV. HPA regulates secretion of glucocorticoids endogenous hormones with potent anti-inflammatory properties. Chronic stress may lead to decreased glucocorticoid sensitivity and impairment in the ability of HPA axis to regulate the immune system. A potential role

of HPA axis in HIV pathogenesis has been reported. Elevated morning cortisol has been associated with rapid disease progression.

An association has been shown between psychological stress, mood and HIV progression, which is probably mediated by molecular messengers of the HPA axis and autonomic nervous system. Besides, HIV progression has been shown to be linked with sympathetic nervous system through various pathways. Lower morning cortisol and flatter diurnal rhythms are associated with greater activation of CD4<sup>+</sup> and CD8<sup>+</sup> T cells (Deepak Nilsoge Guruswamy *et al.*, 2017).

The World Health Organization estimates that 14.8 million women are living with human immunodeficiency virus (HIV) type 1 infection and that another 6.2 million women have died of AIDS. Unprotected vaginal intercourse is the most common route through which women are infected with HIV-1. In sexually active women, the levels of estragon and progesterone vary significantly under different natural and therapeutic conditions. During the monthly reproductive cycle, estragon levels steadily rise during the follicular phase and then fall after ovulation during the luteal phase, at which time progesterone levels rise. Women with low circulating levels of estragon secondary to natural menopause or to therapy with depo-medroxyprogesterone acetate (DMPA) are more likely to become infected with HIV. It is reported that estragon may reduce transmission of HIV-1 across the vaginal epithelium and/or suppress viral replication after transmission has occurred (Karim R *et al.*, 2013).

Lack of estragon increases bone resorption, as well as decreasing the deposition of new bone that normally takes place in weight-bearing bones. The amount of estragon needed to suppress this process is lower than that normally needed to stimulate the uterus and breast gland. Estragon down regulates many of the pro-inflammatory cytokines (Tumour necrosis factor alpha, Interleukin-1, Interleukin-6) that increase bone resorption. These pro-inflammatory cytokines have all been found to be elevated in HIV+ individuals and may not be completely suppressed after ART (Nkiruka1 RU *et al.*, 2017). Estragon appears to down-regulate bone-marrow cell expression of receptor activator of nuclear factor kappa-B ligand (RANKL), and up-regulate gene expression and protein synthesis of osteoprotegerin (OPG). In pre-menopausal subjects, estragon could attenuate the effects of pro-inflammatory cytokines and RANKL

production on osteoclast genesis, thereby mitigating the accelerated bone demineralization associated with HIV infection and treatment. However, the decline in estradiol levels that accompanies menopause would be expected to exacerbate any cytokine-mediated increase in bone (Nkiruka *et al.*, 2017).

### **Humoral response To HIV**

The humoral immune response occurs later in infection; therefore, the level of antibodies during the acute infection is very low. Non-neutralising antibodies to structural proteins (i.e. P17 and P24) are first to appear and generally do not persist. Later neutralising antibodies specific to proteins, involved in the entry of the virus into the cells, will be generated.

### **Materials and Methods**

HIV-1 enters the central nervous system (CNS) during the early stages of HIV infection<sup>1</sup> and has been associated with neurological and neuropsychiatric effects, including major depressive disorder (MDD) and cognitive impairment (CI).

HIV-1 infection targets the central nervous system in subcortical brain areas and leads to high rates of delirium, depression, opportunistic central nervous system infections, and dementia. Long-term HIV replication in the brain occurs in astrocytes and microglia, allowing the virus to hide from antiviral medication and later compromise neuronal function. The associated cognitive disturbance is linked to both viral activity and inflammatory and other mediators from these immune cells that lead to the damage associated with HIV-associated neurocognitive disorders, a general term given for these disturbances. We review the severity and prevalence of the

neuropsychiatric complications of HIV including delirium, neurobehavioral impairments (depression), minor cognitive-motor dysfunction, and HIV-associated dementia. When examining severity of major depression of HIV/AIDS, most of the studies focus on the association of mood disorders with higher rates of disease transmission, lower rates of compliance, and psychological distress from the disease. Major depression makes individuals more susceptible to contracting HIV and AIDS because of its effect on behaviour. Depression factors into HIV risk since it often impacts insight and judgment in decision-making and may exacerbate substance abuse (Eggers C *et al.*, 2017).

## Results and Discussion

HIV associated neurocognitive disorder (HAND) was studied by 8 studies either alone or as mixed diagnosis out of which 7 studies reported mild to severe HAND when compared either with healthy control or within HIV positive patients (Kumar *et al.*, 2019; Yusuf *et al.*, 2017; Balaini *et al.*, 2017; Estiasari *et al.*, 2015; Habib *et al.*, 2013; Achappa *et al.*, 2013; Wang *et al.*, 2013). Only a single study conducted by Nyongesa *et al.*, (2018) reported no significant effect of HIV over neurocognitive skills. Out of 8 studies, 6 studies included patients on HAART for different duration and majorly reported no response. While Balaini *et al.*, 2017 and Nyongesa *et al.*, 2018 found no association between HAND and cART regimen, studies conducted by Yusuf *et al.*, 2017, Achappa *et al.*, (2013), Wang *et al.*, (2013) found mild to severe HAND prevalence irrespective of HAART administration. The positive effect of long term administration of ART over HAND was recorded by Kumar *et al.*, (2019) whereas study performed by Estiasari *et al.*, (2015) reported poor cognitive performance and high

Prevalence rate in absence of HAART treatment. In case of HAND major factors that were found to be associated with poor cognitive performance were long duration of HIV diagnosis, low CD4 count, low educational status, severity of illness, psychiatric diseases and substance use, anemia, low body mass index, increasing age, and female gender.

A total of 6 studies assessed depression and anxiety in PLHIV where 5 studies recorded high prevalence (Adeoti *et al.*, 2018; Ramachandra and Badiger, 2018; Hafeez T, 2018; Betancur *et al.*, 2017; Tesfaw *et al.*, 2016) and one showed no significant occurrence (Gauran *et al.*, 2018). All these studies included the patients on ART for variable duration, hence higher prevalence of depression and anxiety in these patients indicate no significant effect of treatment. Major correlates demonstrated by these studies include female gender, age, smoking, homosexuality, unprotected sex, unemployment, low CD4 count, non-disclosure of HIV status, perceived HIV stigma, poor social support, HIV stage III, poor medication adherence, divorce, and co-morbid TB illness.

Neuropsychological disorders in PLHIV were largely related with stressful life events and diminished social support (Leserman *et al.*, 2002; Ironson *et al.*, 2005). The present review also observed that major correlates for enhanced neuropsychological disorders involve social factors such as being female, HIV stigma, low education and income status, societal isolation, poor family support, smoking and substance use. Larger vulnerability of females towards mental disorders can be attributed to factors such as increased exposure to acute life events, lower social status and network, and financial problem (NACA, 2012). HIV stigma serves as one of the leading factor in increased

preponderance of depression and anxiety. Stigma results in enhanced fatigue levels, isolation, loneliness and feeling of worthlessness (Rodkjaer *et al.*, 2010; Bhate and Munjal, 2014; Berhe and Bayray, 2013). Similarly, social relationship domain not only help in preventing mental disorders but also significantly affect overall QoL in PLHIV as it provides safety, security and financial support. Smoking and substance use bidirectionally indicate status of mental problems as well as disease progression and therefore interventions to stop them are inherent part of HIV management (Chang *et al.*, 2017; Ruggles *et al.*, 2017).

Based upon the present review, the role of HAART in reducing the prevalence of neuropsychological disorders with disease progression is largely meager. This poor effect of HAART can be attributed to irreversible CNS damage occurred during the early disease course before the start of intervention, sustained neuroinflammation, viral replication and load in CNS while on HAART (Becker *et al.*, 2011; Dahl *et al.*, 2014). In- addition, an observational study also demonstrated the neurotoxic effect of HAART specifically by the antibiotics used as first line of treatment (Bacchus *et al.*, 2013). Patients CD4 count also serve as a prognostic factor for HAART response against mental disorders as a low or nadir CD4 count indicate advanced disease state and immune damage.

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