Editorial

Human immunodeficiency virus and the endocrine system

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UNAIDS estimates that there are 33.3 million (31.4 million–35.3 million) people living with HIV at the end of 2009, as compared to 26.2 million (24.6 million–27.8 million) in 1999.[1] This represents a huge 27% increase and implies that more attention should be paid to the medical management of the condition and its comorbidities. Although the incidence of new HIV infections has fallen since the late 1990s, this decrease is offset by the reduction in mortality due to better access to and improved quality of antiretroviral therapy.

As acute complications of HIV decrease, focus has to shift to chronic complications of the disease and chronic adverse effects of current treatment regimes. The estimated number of children living with HIV has also increased to 2.5 million (1.7 million–3.4 million) in 2009,[1] representing a segment of population which will require long-term care.

In Asia, an estimated 4.9 million (4.5 million–5.5 million) people have HIV (2009),[1] of whom 360,000 (300,000–430,000) people are newly infected. While the HIV prevalence is increasing in countries such as Bangladesh, Pakistan, and the Philippines, the incidence has fallen by more than 25% in India, Nepal, and Thailand between 2001 and 2009. The epidemic has remained stable in Malaysia and Sri Lanka during this time period.

Many countries with a high burden of HIV infection also face burgeoning epidemics of non communicable diseases including diabetes.[2] People living with HIV often also have high rates of non communicable diseases. People with HIV are living longer and develop non-HIV-related chronic conditions similar to the general population. They are also more prone to non-infectious diseases because of the nature of HIV (lipodystrophy), anti-retroviral drugs (hyperglycemia, metabolic syndrome), and opportunistic diseases (HIV-associated lymphoma, cervical cancer). HIV positive people have significantly higher rates of hypertension, diabetes, and obesity than those who are HIV negative.[3]

As we try to strengthen and expand diabetes care and other chronic disease services, we must focus on the endocrinopathies associated with HIV/AIDS. We should also learn from the success stories of the AIDS pandemic and include best practices used by HIV programs in our projects. Approaches (peer programs, defaulter tracing initiatives, multidisciplinary teams and community engagement), tools (registers, charts, forms and medical records) and systems (monitoring and evaluation, improving quality, supply chain and procurement, referring people and processing of specimens) which have been shown to be effective should be utilized in the chronic endocrine care programs.[4] Integrated chronic disease clinics that provide continuous care services to people, including those living with HIV and those with noncommunicable diseases, should be encouraged. This will help focus attention on the endocrine and metabolic complications of HIV infection.

HIV is associated with multiple endocrine and metabolic disorders. The association of HIV with diabetes is well described.[5] Diabetes may be present prior to HIV infection or may develop after onset of HIV. Insulin resistance, rather than insulin deficiency, is usually implicated in the pathogenesis of diabetes in HIV-infected patients. While according to earlier reports, evidence of islet cell autoimmunity, or beta cell destruction has not been seen in

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HIV patients,[6] the major contributor to hyperglycemia in HIV/AIDS is iatrogenic. This glucose tolerance may be due to highly active antiretroviral therapy (HAART) or due to other drugs. In this issue, South Asian guidelines compiled by experts from six countries have been published. These guidelines deal with the pathophysiology, screening, diagnosis, and management of diabetes in HIV–infected individuals.[7]

Other components of the metabolic syndrome are noted in HIV. HAART has led to an increase in metabolic dysfunction, including insulin resistance, diabetes, dyslipidemia, and lipodystrophy.[8] Insulin resistance, visceral adiposity, peripheral lipodystrophy, dyslipidemia, and glucose intolerance can occur singly or in combination. This constellation of clinical features is known as the lipodystrophy syndrome. Lipodystrophy may occur with HAART and needs to be treated aggressively in order to minimize cardiovascular morbidity. "Endocrine" drugs such as tesamorelin (a growth hormone releasing factor) are being used to manage this condition.[9]

HIV is also associated with various endocrine abnormalities including those of the growth hormone axis. These include deficiency of growth hormone as well as growth hormone resistance. Growth hormone deficiency may contribute to insulin resistance in HIV-infected patients.[10]

Comparatively, less attention is paid to the other glandular dysfunctions noted in HIV. Hypopituitarism, galactorrhea, unexplained hyponatremia, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and central diabetes insipidus have been noted. Multiple pathophysiologic and drug induced mechanisms have been proposed to explain these abnormalities. These include infection with *Toxoplasma gondii*,[11] *Pneumocystis jiroveci*,[12] or the use of trimethoprim.[13]

Thyroid disorders found in HIV include sick euthyroid syndrome, subclinical hypothyroidism (3.5-12.2%).[14] Grave's disease due to the immune reconstitution syndrome,[15] and thyroiditis due to *Cryptococcus neoformans*, *Pneumocystis jiroveci*, and visceral leishmaniasis.[16] Thyroid function may also be disturbed by lymphoma and Kaposi's sarcoma.

Hypogonadism is another common endocrine disorder in HIV. Low CD4 cell count, advanced illness, medication use, and weight loss are associated with low testosterone levels. Serum free testosterone is suggested as a marker of testicular function.[17] Hypogonadism is hypogonadotrophic in etiology in 75% patients,[18] but may be due to primary testicular failure,[16] including tubercular orchitis.[18]

A high incidence of sexual dysfunction including erectile dysfunction[19] and early 'andropause'[20] has been reported. Frequent menstrual disturbances including prolonged amenorrhea[21] have also been reported.

The most affected gland in HIV, however, is the adrenal gland. While Cushing's syndrome has been reported,[22] Addison's disease is thought to be the commonest endocrinopathy in HIV.[23]

Cytomegalovirus, Kaposis's sarcoma, cryptococcosis, tuberculosis, toxoplasmosis[23] have been reported to affect HIV–infected adrenal glands. Ketoconazole and rifampicin may lead to impaired adrenal function as well.

Many of these endocrine disturbances can easily be treated to help patients achieve a better quality of life. Others, such as adrenal insufficiency, may be potentially life-threatening if not managed appropriately. The increased cardiovascular risk associated with lipodystrophy also needs to be addressed properly. All this can be done effectively, if endocrinologists are involved in the active management of HIV. Both endocrine and HIV specialists should be sensitized to the need for team work. The guidelines on management of diabetes in HIV are a step forward in this direction.

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