Short Commentary **Open Access**

The Emerging Link between HIV Therapy and Diabetes

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Abstract

The screening for the management of diabetes mellitus must be included into regular HIV clinical care and clinicians must consider the metabolic effects of *combinatorial* drug *therapy* for HIV infection and its outcome. Studies are desirable to conclude the pathophysiologic explanation for the high prevalence of diabetes among HIV-infected who are on ART, and cohort studies with significant sample size are required to support.

Keywords: HIV; Diabetes; Diabetes mellitus; Glucose intolerance; Antiretroviral therapy; CD4 lymphocyte; Glucose transporter

Abbreviations DM: Diabetes Mellitus; ART: Antiretroviral Therapy

The Link between HIV and Diabetes

The introduction of highly active antiretroviral therapy has considerably reduced the HIV-related morbidity and mortality by reducing viral load and number of opportunistic infections, enhancement in CD4 lymphocyte counts and span of hospital reside [1]. These improvements have increased the incidences on associated adverse metabolic effects [1,2] and HIV-infected patients frequently experience metabolic complications such as insulin resistance and increasing the risk of diabetes mellitus (DM) [3,4].

The occurrence of diabetes mellitus (DM) has been reported in a range from 2-14% in HIV-infected patients and these statistics vary majorly because of differential diagnosis and composition of the cohort taken with contradictory data on link between HIV infection and DM [5-7]. Some reports consider it as an autonomous risk factor for DM, as number of reports showing enhanced risk and others showing no independent effect of HIV on DM or showing an inverse effect [8-10].

Preclinical studies have demonstrated that the risk of DM increases with the onset of antiretroviral therapy (ART) [11]. Studies have shown consistency with ART-associated type 2 diabetes while supportive studies for islet autoimmunity are markedly rare in patients with ART-associated diabetes. HIV-1 infected patients on continuing ART treatment had 5 fold larger ratios for glucose related metabolic disorders than control composite of HIV negative adults [12].

In a cross-sectional study, the HIV infected patients on ART treatment are reported to have significantly elevated occurrence of glucose metabolism disorders (32.7%) vs. (7.2%) and frank diabetes mellitus (18%) *vs.* (5.2%), than HIV negative adults. CD4+ T-cell counts were one of the factors that was significantly associated with glucose metabolism disorders which were significantly higher even after adjusting other factors like sex, age, obesity and socioeconomic status. Only few patients <25% were aware of their diagnosis of diabetes mellitus in the study [12].

The protease inhibitors (PIs), specific medication on DM risk, increase insulin resistance through the mechanism of insulin resistance and appears to involve in hindrance with glucose transport: photo-affinity labeling with established binding of sequences within the common peptido-mimetic core of HIV protease inhibitors to the major glucose transporter (GLUT4) [13]. There was five to nine fold elevated prevalence of type 2 diabetes in a cross sectional study conducted in 32 centers with metabolic syndrome in 788 HIV infected patients with protease inhibitors medication [6].

The increase of risk of diabetes was considerably high due to collective exposure of stavudine in treatment with zidovudine and diadanosine. The collective exposure of drugs is reported to have adverse events linking with new onset of diabetes in HIV infected patients [13]. It is, therefore, now an important prerequisite for continued monitoring and classification of toxicity and prolonged side effects of the therapy (Figure 1).
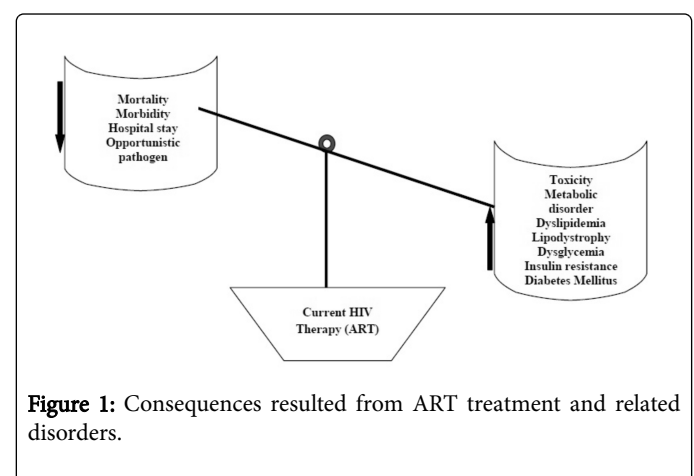
Figure 1: Consequences resulted from ART treatment and related disorders.

There is a proven link between nucleoside analogs to insulin resistance and related dysfunction [14]. However, there is no proven link between analog substitutions and its clinical implications in the

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diabetes. Furthermore, it is known that some factors including positive family history, older age, obesity, lipodystrophy and genetic factor are noticeably related with DM. Unfortunately, these factors have not been thoroughly collected and integrated in the cohort analyses so far.

Further investigations are needed to determine the role and relationship of immune dysfunction, risk of glucose metabolism disorder and diabetes during the due course of HIV infection. The screening for the management of diabetes mellitus must be included into regular HIV clinical care and clinicians must consider the metabolic effects of combinatorial drug therapy for HIV infection and its outcome. Conclusively, studies are desirable to conclude the pathophysiologic explanation for the high prevalence of diabetes among HIV-infected who are on ART, and cohort studies with significant sample size are required to support.

Competing Interests

The author(s) declare that they have no competing interests.

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