

Abstract:

Background: Although glucose abnormalities have been associated with use of protease inhibitors (PIs), other factors may contribute to the development of diabetes mellitus (DM) in HIV-infected patients (pts). To delineate risk factors for DM, we conducted a case-control study in an urban HIV clinic. **Methods:** Incident diagnoses of DM among pts in active follow-up were identified (cases) excluding DM induced by medications other than PIs. 2 controls per case were matched on age +/- 5 yrs, race, gender, and length of clinic follow-up. HIV risk factors, family history of DM, hepatitis B (HBV) & C (HCV) infection, antiretroviral use, body mass index (BMI), lipodystrophy (physician diagnosis), CD4 cell counts (nadir and at time of DM diagnosis), HIV viral load (PCR), mean serum alanine aminotransferase levels (ALT) and mean cholesterol were evaluated at or prior to onset of diabetes in cases or the equivalent period of follow-up in controls. Conditional logistic regression was used to identify factors associated with DM. **Results:** From 5/91 to 12/00, we identified 50 cases of DM. 1 case was excluded as no matched controls could be found, leaving 49 cases and 98 controls. Mean time from initial visit to DM diagnosis was 27 months, mean age was 45 yrs, 65% were male, 39% African American, 34% Hispanic, and 27% Caucasian. Compared with controls, cases had a higher mean BMI (30.0 vs. 25.3 Kg/M²; matched odds ratio [OR] 1.20; p < .001), higher mean ALT (66.3 vs. 43.7 U/L; OR 1.01;p=.013), stronger family history of DM (50% vs. 29.1%; OR 3.30;p=.009), and higher prevalence of fat accumulation (29.6% vs. 12.8%; OR 3.40;p=.025). HCV coinfection was more common in cases than controls (51.1% vs. 36.5%; OR 2.10;p=.066), and cases had greater prior/current PI use (71.4% vs. 58.2%;OR 2.30;p=.072). In multivariate analyses, only BMI (OR 1.18 /kg/m²;p=.010), family history (OR 9.41;p=.034), and ALT (OR 1.02 /U/L;p=.047) were associated with DM. **Conclusions:** Although PI use and HCV coinfection may contribute to risk of DM, as shown by others, traditional risk factors (i.e. obesity, family history) account for much of the risk of DM in HIV-infected persons. The association of serum ALT level with DM may reflect liver injury or steatosis, which may predispose to hyperglycemia. These findings suggest that there are complex interrelationships between genetic factors, treatment-induced metabolic changes, and liver injury in the pathogenesis of DM in HIV-infected pts.

Background:

- Metabolic and endocrine abnormalities have been seen in-patients infected with HIV, including lipid and glucose abnormalities.
- Incidence of new-onset diabetes mellitus, clinically similar to type 2 diabetes, has ranged from 1%-7% in various studies [1].
- Although clinical and in vitro studies have demonstrated a direct effect of PIs on glucose metabolism, other factors may contribute to the development of DM in HIV-infected patients [2-4].
- For example, HCV co-infection could be a risk factor for DM as has been reported in the general population [5].

Objective: To identify potential risk factors for DM in HIV-infected persons.

Methods:

- We performed a retrospective, case control study by reviewing computer-based medical records in the Center for Special Studies clinic at New York Presbyterian Hospital-Cornell which has provided care for approximately 5400 HIV-infected patients from May 1991 to Dec 2000.
- Inclusion criteria: patients with a clinic visit within the prior 6 months, incident diagnoses of DM based on the WHO definition.
- Exclusion criteria: medication induced DM other than PIs (corticosteroid, megestrol acetate, growth hormone, pentamidine use), acute/chronic pancreatitis.
- Two controls to one case were matched on age (+/- 5 years), race, gender, and length of clinic follow-up (+/- 24 weeks). 2 female patients were unable to be matched on gender or race, 1 male patient, unable to be matched on gender, 1 male patient unable to be matched on time of initial visit for 1 control patient, so time of first visit for control was extended for -52 weeks.
- Demographic information was extracted. Patients whose family history was not documented were queried at clinic visits.
- To determine lipodystrophy syndrome, patients' physicians assessed fat redistribution, lipotrophy, fat accumulation.
- Factors such as HBV & HCV serostatus, antiretroviral use, body mass index (BMI), absolute CD4 count (nadir and at time of DM diagnosis), HIV viral load (PCR), mean ALT and mean cholesterol level were evaluated at or prior to onset of diabetes in cases or the equivalent period of follow-up in controls.

- Matched odds ratios were calculated by conditional logistic regression. Rank tests were performed on continuous variables with

Results:

- There was a 2.4% prevalence of DM in HIV-infected pts.
- 62 were incident cases of diabetes diagnosed over 8 months, 18 were diagnosed on growth hormone or megestrol acetate use.
- One patient was excluded because no matched control was available with 98 control patients without DM.
- Mean time of clinic follow-up from initial visit to DM diagnosis was 27 months (range 6-43 months).

Table 1: Patient Characteristics

n	Cases n=49
Gender:Male(%)	31 (63%)
Female (%)	18 (37%)
Age, yrs,mean(SD)	45.1 (7.5)
Race(%)	
African American	19 (39%)
Hispanic	17 (35%)
Caucasian	13 (27%)
HIV Risk Factor	
IVDU (%)	23 (47%)
Other (%)	26 (53%)
Year of HIV diag.	1991
Median (IQR)	(1989-1995)
BMI [Kg/M²] at DM diag²	
Mean (SD)	30.0 (6.3)
Median (IQR)	28.5(25-34)
Immediate Family history DM³ (%)	24 (50%)
+HCV antibody ⁴ (%)	24 (51%)
+HBsAg ⁵ (%)	2 (4%)
Cholesterol ⁶ [mg/dL]	
Mean (SD)	171.7(50.6)
Random triglyceride ⁷ [mg/dL]	
Mean (SD)	337.8(281.9)
Median (IQR)	262.3(166.5-401.5)
ALT [U/L]⁸ Mean (SD)	66.3(56.8)
Nadir CD4,cellsx10 ³ /L	
Median (IQR)	173(34-325)
CD4,cellsx10 ³ /L at DM diag	
Median (IQR)	331 (214-500)
HIV RNA, log ₁₀ copies/ml at DM diag.	
Mean (SD)	2.5(1.15)
NRTI use (%)	40(81.6)
NNRTI use (%)	5(10.2)
PI use (%)	35 (71%)
Time, months, from start PI to DM diag.	
Mean (SD)	22.6(10.3)
Lipodystrophy (%)	9 (18%)
Fat accumulation⁹ (%)	13 (30%)