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Predictors of insulin resistance among Hispanic adults infected with or at risk of infection with the human immunodeficiency virus and hepatitis C virus

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- iii. Carmen Castaneda-Sceppa does not own stocks or shares.
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Summary

Both the human immunodeficiency (HIV) and hepatitis C (HCV) viruses have been associated with insulin resistance (IR). However, our understanding of the prevalence of IR, the underlying mechanisms and predisposing factors is limited, particularly among minority populations. We conducted a study of 333 Hispanic adults including: 76 HIV-monoinfected, 62 HCV mono-infected, 97 HIV/HCV co-infected, and 98 uninfected controls with a specific focus on HCV infection and liver injury as possible predictors of IR. IR was measured using the QUICKI index. The majority (55% to 69%) of participants in all groups had QUICKI values <0.350 . Body mass index was associated with IR in all groups. Triglycerides were associated with IR in the uninfected control group only (-1.83 , $SE = 0.58$, $p=0.0022$). HCV was associated with IR in participants infected with HIV (-0.012 , $SE = 0.0046$, $p=0.010$). Liver injury, as measured by FIB-4 score, was significantly associated with IR independently of HCV infection (-0.0035 , $SE=0.0016$, $p=0.027$). In the HIV/HCV co-infected group, treatment with nucleoside reverse-transcriptase inhibitors plus non-nucleoside reverse-transcriptase inhibitors (-0.021 , $SE=0.080$, $p=0.048$), but not protease inhibitors (-0.000042 , $SE=0.0082$, $p=0.96$) was associated with IR. HCV infection and antiretroviral agents, including NRTI plus NNRTI treatment are contributors to IR in HIV infection. Liver injury, as measured by the FIB-4 score, is a predictor of IR independently of HCV infection.

Keywords

QUICKI; insulin resistance; HIV; HCV; Hispanic; antiretroviral therapy; liver disease

Introduction

In the United States, 15 to 30% of HIV-infected persons are also co-infected with HCV [1]. Both infections disproportionately affect minorities, including Hispanics, now the largest minority group in the US [2–4]. In 2002, HIV was the third leading cause of death among Hispanic men, and the fourth leading cause of death among Hispanic women aged 35 to 44 years [5]. HIV infection accelerates the impact of HCV on liver disease [6–9], and liver disease is an important cause of death among persons with HIV infection [10–12]. Hispanics appear to be more susceptible than other racial groups to HCV-related liver disease progression [13–17], and though the underlying mechanisms are not well understood, diabetes has been implicated [15].

There is strong evidence that HCV infection is associated with type 2 diabetes [18–23]. Population data from the Third National Health and Nutrition Examination Survey (NHANES III) showed that HCV-infected persons 40 years of age and older are more than three times as likely as those without HCV to have type 2 diabetes after other important risk factors are considered, including age, body mass index (BMI), and a history of drug or alcohol abuse [22]. A recently published longitudinal study in Taiwan showed that HCV infection was an independent predictor of diabetes, especially in persons with a high BMI [23], establishing that HCV infection precedes the development of diabetes. HCV has been associated previously with insulin resistance (IR) [24,25], but many studies have lacked data on the role of liver injury.

In the general population, established predictors of IR include age, race/ethnicity and obesity. In persons with HIV, in addition to HCV co-infection, there are other risk factors that may

promote IR, such as antiretroviral therapy [26–30], elevated triglycerides [31,32] and body fat changes, including visceral fat accumulation and peripheral fat atrophy [33–36]. It is possible that Hispanics are more susceptible to these factors than other racial/ethnic groups because of an underlying predisposition to IR [37–40].

In this context, we conducted a study to determine the factors associated with IR among Hispanic adults of Caribbean origin infected with or at risk of HIV/HCV infection. The aims of the present study were: 1) to identify independent predictors of IR in relation to HIV/HCV infection status in this racial/ethnic group, 2) to assess the independent effect of HCV infection on IR and, 3) to determine the role of liver injury on IR.

Methods

Study Population and Data Collection

The data presented here were derived for secondary analyses from the BIENESTAR study, an open enrollment prospective cohort study designed to examine the role of drug use as a cofactor in HIV-related nutritional and metabolic disorders in Hispanic adults. The cohort is comprised of four groups: HIV-infected current drug users, HIV-infected persons who do not use drugs ('non-drug users'), HIV-uninfected current drug users and healthy Hispanic controls.

Recruitment was done through community outreach on the street, in homeless shelters, support groups, and health clinics. Self-identified Hispanic adults (≥ 18 years) who spoke Spanish as their first language were considered eligible. Most participants were of Puerto Rican origin, an ethnic group that is a mix of European (predominant), Black and Amerindian race [41]. The exclusion criteria were: pregnant at recruitment, non-HIV associated malignancies, the use of hormones for a sex change, and refusal to sign a consent form to release medical records. IR was not the main outcome of the BIENESTAR study, but fasting insulin and glucose values were collected for descriptive purposes. The data presented here were from the first study visit for each participant at which fasting insulin and glucose values were available. All participants gave informed consent, and were paid a modest stipend for their participation. The study was approved by the Institutional Review Board at the Tufts Medical Center.

Study interviews were conducted in Spanish by bilingual, Hispanic personnel. Data collected by standardized interview included detailed information on housing, HIV history, HIV medications, and health behaviors including smoking, alcohol consumption, and drug use. Participants were asked to fast for a minimum of five hours prior to the clinic visit, and were asked not to drink alcohol or do strenuous physical exercise for a period of 48 hours prior to the visit. Body weight and height were measured by standardized techniques. BMI was calculated as weight in kilograms divided by height in square meters.

Data were available on waist circumference, suprailliac, and triceps skin folds in 115 HIV-infected participants. These data were used to conduct limited analyses on the role of fat distribution as a predictor of insulin resistance among HIV-infected participants. Central obesity was identified as a waist circumference of >102 cm in men and >88 cm in women [42]. To distinguish visceral adiposity with subcutaneous lipoatrophy from central, subcutaneous obesity [43], visceral adiposity was defined as the presence of central obesity combined with a suprailliac skin fold thickness of <2.0 cm (an *a priori* and arbitrary cutoff). There were four HIV-infected participants (4%) and one HIV-uninfected participant with visceral adiposity using this definition. This was too low a prevalence to reliably examine visceral adiposity in the analyses. Triceps skin fold was examined as a measure of extremity fat and treated as a continuous variable in the analyses. Skin fold thicknesses were measured in triplicate and the mean of the three measures was used in the analyses.

Insulin resistance—Fasting plasma glucose was determined by the hexokinase enzymatic method (Sigma Diagnostics, St. Louis, MO) and insulin levels were determined by radioimmunoassay (ICN Biomedical Inc., Costa Mesa, CA) with CV of 5%. IR was determined using the Quantitative Insulin Sensitivity Check Index –QUICKI, calculated as, $1/[\log(I_0) + \log(G_0)]$, where I_0 is the fasting insulin, and G_0 is the fasting glucose [44]. QUICKI correlates as well or better with IR measured by the euglycemic hyperinsulinemic clamp compared to fasting insulin using the Homeostasis Model Assessment of insulin resistance (HOMA-IR) [44,45]. Mean QUICKI levels in normal populations are reported to range from 0.37 to 0.39 [44,45], and QUICKI tends to decrease with increasing IR. QUICKI values were used on a continuous scale or dichotomized at the cutoff of 0.350, based on previous studies [44,45,46]. Here, for simplicity, IR is used to signify lower QUICKI values.

HIV disease and related variables—Self-reported HIV status was confirmed by enzyme immunoassay (Genetic Systems™ HIV1 /HIV2 Plus O EIA, Biorad Laboratories, Redmond, WA). HIV RNA levels were measured by reverse transcriptase polymerase chain reaction (PCR) using a Roche Amplicor Monitor (Roche Molecular Systems, Somerville, NJ), with a lower detection limit of 400 copies/mL. An undetectable viral load was given a value of 200 copies/mL, the midpoint between zero and the limit of detection. CD4 cell counts were determined using a specific monoclonal antibody and fluorescence-activated cell sorting analysis.

Antiretroviral regimens—Since there were not enough data to examine individual antiretroviral agents, antiretroviral treatment was treated as a binary variable (yes/no). Therapy was defined as the use of any protease inhibitor (PI), or nucleoside reverse-transcriptase inhibitor (NRTI). These classes were not mutually exclusive. All participants who were taking a NRTI were also taking a NNRTI so these agents could not be evaluated separately. Some (rare) PI users were on PI monotherapy. The duration of use of the class of agent was also examined.

Hepatitis C—Hepatitis C virus (HCV) infection was determined qualitatively by the presence of HCV RNA in serum (AMPLICOR Hepatitis C Virus test, Version 2.0 Roche Molecular Systems Inc., Branchburg, NJ, USA). The number of years with HCV infection was estimated from the reported first use of injection drugs. The presence of hepatitis B virus surface antigen was determined using the HBsAg Enzyme Immunoassay 3.0 (Biorad Laboratories, Redmond, WA, USA). Data from six participants with positive serum tests for HBsAg were set aside to focus the study on HCV infection.

Liver Injury—The liver function tests aspartamine aminotransferase (AST) and alanine aminotransferase (ALT) were routinely collected, but as minor elevations are frequent, liver injury was defined by the FIB-4 score [47], calculated as: $(\text{age [yr]} \times \text{AST [U/L]}) / ((\text{PLT} [10^9/\text{L}]) \times (\text{ALT [U/L]}^{1/2}))$, where PLT corresponds platelet count. FIB-4 values > 3.25 are consistent with significant fibrosis at a sensitivity of 86 to 97% [47,48]. Elevated values of the FIB-4 score in the range of 1.45 to 3.25 may not indicate fibrosis, but have been associated with other sorts of liver biopsy abnormalities including necro-inflammatory activity [47]. FIB-4 was used on a continuous scale in these analyses since we were interested in all sorts of liver injury, including drug toxicity or other processes that can lead to elevated AST or ALT and ultimately, fibrosis. Data for the FIB-4 was collected in the BIENESTAR study beginning September, 2006. Of the 333 participants included in this analysis, 80 (24%) were missing data for FIB-4 score for the reason that the measure had not yet been added to the protocol at the time of the visit.

Statistical Analyses

Statistical analyses were carried out using SAS version 9.1 (SAS Inc., Chicago, IL). Mean and standard deviation (SD) was reported for normally distributed continuous data, median (25th, 75th percentile) for non-normally distributed continuous data, and number and percentage for categorical data. Viral load, insulin and serum triglyceride values were log transformed for analyses. The data were analyzed together, and stratified by HIV/HCV infection status. Differences in participant characteristics in Table 1 were tested with the least square means option in the general linear models procedure (PROC GLM) in SAS for continuous, normally distributed and log transformed data. The Wilcoxon rank sum test was used for non-normally distributed data. Chi-square or Fisher's exact test was used to test between-group differences for categorical variables. Univariate associations between independent variables of interest and QUICKI were determined with Pearson's coefficient of correlation for continuous, normally distributed and log transformed continuous variables or by independent groups t-test for categorical variables (Table 2). Multivariate least squares regression models were used to examine independent determinants of QUICKI expressed on the continuous scale to enhance statistical power (Table 3–Table 5). Adjustment was made for known predictors of IR including age, gender, body mass index, and serum triglycerides. Lifestyle factors including smoking, alcohol consumption and drug use were also evaluated as predictors of IR. HIV disease-related factors including years with HIV, current CD4 count, nadir CD4 count, viral load, and antiretroviral therapy were considered. Variables were included in the multivariate models either because of their known or suspected association with insulin resistance or based on an observed univariate association with QUICKI at a $P < 0.10$. To assess the independent effect of HCV infection and liver injury on IR in HIV/HCV and HIV mono-infected participants separately, the overall study sample was re-stratified into two groups based on HIV infection status (Table 4). Multivariate analyses were used to examine the independent association between HCV infection and QUICKI while adjusting for the variables described above. The data from all groups were then combined to examine the effect of FIB-4 on QUICKI in the subset of 253 subjects for whom FIB-4 data were available. FIB-4 was added to a model with HCV infection to determine if the addition of a variable describing the presence of liver injury would be an independent predictor of QUICKI or would alter the size of the effect estimate for HCV (Table 5). It was not possible to include a term for years with HIV infection in the model since it is undefined for the HIV-uninfected. To evaluate the influence of antiretroviral therapy on QUICKI in this model which included HIV-uninfected subjects, dummy variables combining HIV status plus antiretroviral treatment use were coded as follows: HIV-infected plus PI use; HIV-infected plus NRTI/NNRTI use; HIV-infected plus no antiretroviral use; HIV-uninfected (reference category).

Results

Subject characteristics stratified by HIV/HCV infection status

Subject characteristics stratified by HIV/HCV infection status are shown in Table 1. There were significant between-group differences in age, gender, as well as smoking and drinking habits. Differences in rates of drug use were due to the recruitment strategy. The mean BMI in all groups fell into the overweight category [49], and was highest in the HIV/HCV uninfected (hereafter termed “uninfected” group). Triglycerides were significantly higher in the HIV-infected groups compared to the HCV-mono infected or uninfected groups ($p < 0.001$ for all differences), but not significantly different from each other ($p = 0.57$). Mean QUICKI values for all groups were below 0.350. The average QUICKI level was significantly lower in the HIV/HCV co-infected group compared to each of the other three groups ($p < 0.05$ for all comparisons), but when QUICKI was examined on a categorical scale, based on the 0.350 cutoff, the difference in prevalence of insulin resistance among the groups was not significant. Average FIB-4 scores were highest in the HIV/HCV co-infected group. Of the 19 participants

with FIB-4 >3.25, a value consistent with significant fibrosis, 16 (84%) were HIV/HCV co-infected and 3 (16%) were HCV mono-infected. HIV/HCV co-infected participants had a longer history of HCV and HIV infection than the HCV or HIV-mono infected participants.

Univariate predictors of IR

Table 2 shows the results for univariate associations of IR and the independent variables of interest in the 333 study participants combined as one group. The univariate associations between QUICKI and continuous variables were expressed as correlation coefficients, while for categorical variables, the univariate associations were expressed as a between-group difference in mean QUICKI values. IR was associated with age, body mass index, serum triglycerides, FIB-4 score, HIV-infection and years with HIV infection. Non-drinkers were more IR than drinkers.

Multivariate predictors of IR stratified by HIV/HCV infection status

In independent multivariable analyses for each infection group (Table 3), higher BMI was significantly associated with IR in all four groups. Higher triglycerides were associated with IR only in the uninfected group ($p=0.0022$). In this group alone, current drinking was associated with less IR. Any use of antiretroviral therapy was associated with IR in the HIV/HCV co-infected group, but not in the HIV-mono-infected group. No other variables, including years with HIV infection, CD4 cell counts or nadir CD4 cell count were significant predictors of IR.

The term for antiretroviral therapy was replaced in the models with a term describing either use of PI or NRTI plus NNRTI agents in independent models for each class of antiretroviral agent. The use of a PI or NRTI plus NNRTI was not associated with IR in the HIV mono-infected group. In the HIV/HCV co-infected group, IR was associated with the use of NRTI plus NNRTI (-0.021 , $SE=0.010$, $p=0.048$), but not with the use of PI (-0.00042 , $SE=0.0082$, $p=0.96$). The duration of use of the agent was not significant for either use of NRTI plus NNRTI or use of PI. Of the 173 HIV-infected participants, 49 (28%) were not on any form of antiretroviral therapy. Of the 124 on antiretroviral therapy, 121 (98%) were on a NRTI agent. The NRTI agents used were as follows: AZT, 39 (32%); 3TC, 71 (59%); D4T, 26 (21%) DDI, 16 (13%). Five of the 173 HIV-infected participants were using indinavir.

Effect of HCV infection on IR

Since the stratification used in Table 3 did not allow the assessment of chronic HCV infection as a predictor of IR, the data were re-stratified into two groups: HIV-infected and HIV-uninfected (Table 4). The HIV-infected group included HIV-mono-infected and HIV/HCV co-infected participants, and the HIV-uninfected group included HCV-mono-infected and uninfected participants. Multivariate analyses were run separately in each group with the addition of a term for HCV to the covariates assessed above. Chronic HCV infection was a significant predictor of IR in the HIV-infected ($p=0.019$), but not in the HIV-uninfected participants ($p=0.26$). BMI and triglycerides were also significant predictors IR in both groups.

The effect of liver injury on IR

To examine the effect of HCV and liver injury on QUICKI, the data from the 253 persons for whom FIB-4 data were available were analyzed in models with HCV that included or excluded FIB-4 (Table 5). FIB-4 was a significant predictor of QUICKI in the multivariate analyses, and the addition of FIB-4 to the model with HCV attenuated the effect estimate for HCV by about 23%. However, the term for HCV remained significant in the model that included a term for FIB-4.

The role of extremity fat as a predictor of IR

Greater triceps skinfold thickness was associated with IR ($r = -0.15$, $p = 0.046$) in univariate analyses using data from all groups. In the multivariate analyses shown in Table 3, triceps skin fold was substituted for BMI in models for the HIV-mono-infected ($n = 52$ with triceps skin fold data available) and HIV/HCV co-infected participants ($n = 60$ with triceps skin fold data available). Greater triceps skin fold was associated with IR in the HIV/HCV co-infected group (-0.0020 , $SE = 0.00094$, $p = 0.036$), but was not associated with IR in the HIV-mono-infected group ($p = 0.13$) when other variables, including antiretroviral therapy, were considered in multivariate analyses.

Discussion

The majority of participants in the BIENESTAR cohort were frankly IR as defined by a QUICKI value ≤ 0.350 [44–46]. However, the prevalence of IR was not significantly higher in HIV-infected participants compared with the uninfected controls, and HIV-infection was not an independent predictor of IR when adjusted for other variables in multivariate analyses. These results agree with a previous study conducted by our group in the Nutrition for Healthy Living Cohort [50], in which the rate of IR in HIV-infected participants was 51%, a prevalence that was not significantly different from matched controls derived from the NHANES III study (47%) in analyses adjusted for known predictors of IR. Brown et al. found in the MACS cohort higher rates of elevated insulin among HIV-infected men compared to HIV-uninfected control subjects after adjusting for a variety of risk factors including antiretroviral therapy [51]. In the present study no other HIV-related factors were associated with IR. Other studies have shown a weak association of insulin resistance with higher concurrent or nadir CD4 count [52,53].

In addition to BMI and triglycerides, both of which are recognized risk factors for IR in the general population, predictors of IR in this population included HCV infection and the use of NRTI plus and NNRTI agents, but not PI. The ability of HCV to impact IR was apparent only in the HIV co-infected participants. In this group alone, antiretroviral therapy appeared to be an additional contributor to IR, independently of HCV. These two factors could explain why IR was more common in the HIV/HCV co-infected group compared to the HIV-mono infected group, despite the lower average BMI and triglyceride levels in the HIV/HCV co-infected group. There was no evidence that the effects of HCV infection and antiretroviral therapy act synergistically, though the absence of an effect of antiretroviral therapy in the HIV-mono-infected patients is suggestive. This study may have lacked the statistical power necessary to detect such an effect. Our results confirm previous reports of an effect of HCV on IR [24,25, 42].

The role of liver injury in IR, induced either by HCV or by antiretroviral therapy [53], is not clear. In a multivariate model, both FIB-4 and HCV were independent predictors of IR. The addition of FIB-4 to the model with HCV attenuated the size of the effect estimate for HCV, but only by about 23%, and the term for HCV infection remained significant. These data support the hypothesis that HCV affects IR by a mechanism that is independent of HCV-induced liver damage [54,55]. Studies conducted in a chimpanzee model suggest interplay between cellular lipid metabolism and HCV replication [56].

Our results showed an independent effect of antiretroviral therapy on IR in the HIV/HCV co-infected participants although there was no association of IR with PI in this study. Since PI therapy was associated with IR early in its use [57,58], it is likely that this was specific to select PI agents, such as indinavir, rather than to the class as a whole. NRTI and NNRTI class agents have also been associated with IR [50,51,59,60]. The elevation of serum lactate by NRTI has been proposed as an explanatory mechanism for NRTI-related IR [59]. Lactate levels were not collected in this study. Our data do not support an important role for peripheral lipotrophy in

IR. This result agrees with that of Meininger and colleagues [61] who found that low extremity fat was a predictor of IR only among HIV-infected men with lipodystrophy, but not among HIV-infected men without lipodystrophy. It also agrees with a recent study by Blumer et al., showing NRTI-related IR may develop in persons showing no alterations in body composition [60].

This study has numerous strengths. The participants were recruited from the community as opposed to a clinic-based sample, and therefore the data should be representative of the target population, and without reference to the presence of self-perceived lipodystrophy. A healthy control group was included in this study and evaluated by the same team using the same measures. The study was restricted to Hispanics, which gives the study high internal validity. Factors associated with HCV infection, which have been lacking in previous studies, including liver injury, HIV infection, drug use and other lifestyle factors were measured and evaluated in these analyses.

Limitations of the study include the cross-sectional design, which cannot establish the temporal relationship between HCV infection and IR. IR was measured using a surrogate and not the euglycemic hyperinsulinemic clamp technique [62], considered the gold standard, which may have resulted in some misclassification. The extent of liver injury was not determined using liver biopsies. Finally, the generalizability of our findings may be limited given that only Hispanic subjects were included.

In conclusion, the prevalence of frank IR is high in this group of Hispanic adults, but not higher in person infected with HIV. Our findings contribute to a growing body of evidence that HCV has an important role in IR in the context of HIV. This study also suggests that the effect of HCV on IR is independent of liver injury. Antiretroviral therapy including NRTI agents appears to promote IR in HIV-infected Hispanics independently of obvious alterations in fat distribution. Further studies are needed to clarify the underlying mechanisms. Since HIV, HCV and IR disproportionately affect Hispanics in the US, physicians should routinely monitor this high-risk population, including HCV-infected patients with no apparent liver disease, and encourage exercise, weight control and other interventions that promote insulin sensitivity. Other culturally appropriate interventions, including dietary interventions, to reduce IR in this population are needed.

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C.W. contributed to the interpretation of the data and the preparation of the manuscript.

J.E.F. contributed to the study design, data collection, analyses, interpretation of the data and writing of the manuscript.

References

1. Sherman KE, Rousier SD, Chung RT, Rajicic N. Hepatitis C Virus prevalence among patients infected with Human Immunodeficiency Virus: a cross-sectional analysis of the US adult AIDS Clinical Trials Group. *Clin Infect Dis* 2002;34:831–837. [PubMed: 11833007]
2. Therrian, M.; Ramirez, RR. Current Population Reports. Washington DC: US Department of Commerce, Bureau of the Census; 2001. The Hispanic population in the United States: March 2000; p. 20-535.

3. Cheung RC, Currie S, Shen H, Ho SB, et al. Chronic hepatitis C in Latinos: natural history, treatment eligibility, acceptance, and outcomes. *Am J Gastroenterol* 2005;100:2186–2193. [PubMed: 16181367]
4. Tedaldi EM, Hullsiek KH, Malvestutto CD, et al. Prevalence and characteristics of hepatitis C virus coinfection in a human immunodeficiency virus clinical trials group: the Terry Bein Community Programs for Clinical Research on AIDS. *Clin Infect Dis* 2003;36:1313–1317. [PubMed: 12746778]
5. Anderson, RN.; Smith, BL. HIV Deaths: Leading causes for 2002; National Vital Statistics Report [online serial]. 2005 Mar 7. p. 1-90. Available from: http://www.cdc.gov/nchs/data/nvsr/nvsr53/nvsr53_17.pdf
6. Eyster ME, Diamondstone LS, Lien JM, et al. Natural history of hepatitis C virus infection in multitransfused hemophiliacs: effect of coinfection with human immunodeficiency virus. The Multicenter Hemophilia Cohort Study. *J Acquir Immune Defic Syndr* 1993;6:602–610. [PubMed: 8098752]
7. Darby SC, Ewart DW, Giangrande PL, et al. Mortality from liver cancer and liver disease in haemophilic men and boys in UK given blood products contaminated with hepatitis C. *The Lancet* 1997;350:1425–1431.
8. Torre D, Tambini R, Cadario F, et al. Evolution of coinfection with human immunodeficiency virus and hepatitis C virus in patients treated with highly active antiretroviral therapy. *Clin Infect Dis* 2001;33:1579–1585. [PubMed: 11588701]
9. Allory Y, Charlotte F, Benhamou Y, et al. Impact of human immunodeficiency virus infection on the histological features of chronic hepatitis C: a case-control study. MULTIVIRC group. *Human Pathol* 2000;31:69–74. [PubMed: 10665916]
10. Bica I, McGovern B, Dhar R, et al. Increasing mortality due to end-stage liver disease in patients with human immunodeficiency virus infection. *Clin Infect Dis* 2001;32:492–497. [PubMed: 11170959]
11. Konopnicki D, Mocroft A, de Wit S, et al. Hepatitis B and HIV: prevalence, AIDS progression, response to highly active antiretroviral therapy and increased mortality in the EuroSIDA cohort. *AIDS* 2005;19:593–601. [PubMed: 15802978]
12. Tatsunami S, Taki M, Shirahata A, Mimaya J, Yamada K. Increasing incidence of critical liver disease among causes of death in Japanese hemophiliacs with HIV-1. *Acta Haematologica* 2004;111:181–184. [PubMed: 15153708]
13. Bonacini M, Groshen MD, Yu MC, et al. Chronic hepatitis C in ethnic minority patients evaluated in Los Angeles County. *Am J Gastroenterol* 2001;96:2438–2441. [PubMed: 11513187]
14. Hoyumpa A, Sharkey F, Page R, et al. Greater prevalence of cirrhosis in Hispanics than in Caucasians or African Americans [Abstract]. *Hepatology* 2005;42:442.
15. Verma S, Bonacini M, Govindarajan S, et al. More advanced hepatic fibrosis in Hispanics with chronic hepatitis C infection: role of patient demographics, hepatic necroinflammation, and steatosis. *Am J Gastroenterol* 2006;101:1817–1823. [PubMed: 16790034]
16. Lepe R, Layden-Almer JE, Layden TJ, Cotler S. Ethnic differences in the presentation of chronic hepatitis C. *J Viral Hepatitis* 2006;13:116–120.
17. Cheung RC, Currie S, Shen H, et al. Chronic hepatitis C in Latinos: natural history, treatment eligibility, acceptance, and outcomes. *Am J Gastroenterol* 2005;100:2186–2193. [PubMed: 16181367]
18. Allison ME, Wrehitt T, Plamer CR, et al. Evidence for a link between hepatitis C virus infection and diabetes mellitus in a cirrhotic population. *J Hepatology* 1994;21:1135–1139.
19. Ozyilkan E, Erbas T, Simsek H, et al. Increased prevalence of hepatitis C virus antibodies in patients with diabetes mellitus. *J Intern Med* 1994;253:283–284. [PubMed: 8120528]
20. Fraser GM, Harman I, Meller N, et al. Diabetes mellitus is associated with hepatitis C but not chronic hepatitis B infection. *Isr J Med Sc* 1996;32:526–530. [PubMed: 8756978]
21. Caronia S, Taylor K, Pagliaro L, et al. Further evidence for an association between non-insulin dependent diabetes mellitus and chronic hepatitis c virus infection. *Hepatology* 1999;30:1059–1063. [PubMed: 10498660]
22. Mehta SH, Brancati FL, Sulkowski MS, et al. Prevalence of type 2 diabetes mellitus among persons with hepatitis C virus infection in the United States. *Ann Intern Med* 2000;133:592–599. [PubMed: 11033586]

23. Wang CS, Wang ST, Yao WJ, Chang TT, Chou P. Hepatitis C virus infection and the development of type 2 diabetes in a community-based longitudinal study. *Am J Epidemiol* 2007;166:196–203. [PubMed: 17496314]
24. Duong M, Petitie JM, Piroth L, et al. Association between insulin resistance and hepatitis C virus chronic infection in HIV-hepatitis C virus co-infected patients undergoing antiretroviral therapy. *J Acquir Immune Def Syndr* 2001;27:245–250.
25. Howard AA, Yungtai L, Floris-Moore M, et al. Hepatitis C virus infection is associated with insulin resistance among older adults with or at risk of HIV infection. *AIDS* 2007;21:633–641. [PubMed: 17314526]
26. Tsiodras S, Mantzoros C, Hammer S, Samore M. Effects of protease inhibitors on hyperglycemia, hyperlipidemia, and lipodystrophy. *Arch Intern Med* 2000;160:2050–2056. [PubMed: 10888979]
27. Justman JE, Benning L, Danoff A, et al. Protease inhibitor use and the incidence of diabetes mellitus in a large cohort of HIV-infected women. *J Acquir Immune Def Syndr* 2003;32:298–302.
28. Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the Multicenter AIDS Cohort Study. *Arch Intern Med* 2005;165:1179–1184. [PubMed: 15911733]
29. Murata H, Hruz PW, Mueckler M. The mechanism of insulin resistance caused by HIV protease inhibitor therapy. *J Biol Chem* 2000;275:20251–20254. [PubMed: 10806189]
30. Noor MA. The role of protease inhibitors in the pathogenesis of HIV-associated insulin resistance: cellular mechanisms and clinical implications. *Current HIV/AIDS Reports* 2007;4:126–134. [PubMed: 17883998]
31. Grunfeld C, Kotler DP, Hamadeh R, Tierney A, Wang J, Pierson RN. Hypertriglyceridemia in the acquired immunodeficiency syndrome. *Am J Med* 1989;86:27–31. [PubMed: 2910092]
32. El Sadr WM, Mullin CM, Carr A, et al. Effects of HIV disease on lipid, glucose and insulin levels: results from a large anti-retroviral naive cohort. *HIV Medicine* 2005;6:114–121. [PubMed: 15807717]
33. Lo JC, Mulligan K, Tai VW, Algren H, Schambelan M. Body shape changes in HIV-infected patients. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;19:307–308. [PubMed: 9803975]
34. Carr A, Samaras K, Burton S, et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. *AIDS* 1998;12:F51–F58. [PubMed: 9619798]
35. Carr A, Samaras K, Thorisdottir A, Kaufmann GR, Chisholm DJ, Cooper DA. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. *Lancet* 1999;353:2093–2099. [PubMed: 10382692]
36. Saint-Marc T, Partisani M, Poizot-Martin I, et al. Fat distribution evaluated by computed tomography and metabolic abnormalities in patients undergoing antiretroviral therapy: preliminary results of the LIPOCO study. *AIDS* 2000;14:37–49. [PubMed: 10714566]
37. Stern MP, Gaskill SP, Hazuda HP, Gardner LI, Haffner SM. Does obesity explain excess prevalence of diabetes among Mexican Americans? Results of the San Antonio Heart Study. *Diabetologia* 1983;24:272–277. [PubMed: 6862133]
38. Palaniappan LP, Carnethon MR, Fortmann SP. Heterogeneity in the relationship between ethnicity, BMI and fasting insulin. *Diabetes Care* 2002;25:1351–1357. [PubMed: 12145234]
39. Tull ES, Thurland A. Dyslipidemia and insulin resistance in relation to genetic admixture among Hispanics and non-Hispanic blacks of Caribbean origin. *J Natl Med Assoc* 2004;96:332–340. [PubMed: 15040515]
40. Bermudez OI, Tucker KL. Total and central obesity among elderly Hispanics and the association with type 2 diabetes. *Obesity Res* 2001;9:443–451.
41. Choudhry S, Coyle NE, Tang H, et al. Genetics of Asthma in Latino Americans GALA Study. Population stratification confounds genetic association of studies among Latinos. *Hum Genet* 2006;118:652–664. [PubMed: 16283388]
42. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Survey. *JAMA* 2002;16:356–359. [PubMed: 11790215]
43. Kotler DP. HIV Infection and lipodystrophy. *Progress in Cardiovascular Diseases* 2003;45:269–284. [PubMed: 12638091]

44. Katz A, Nambi SS, Mather K, et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab* 2000;85:2402–2410. [PubMed: 10902785]
45. Bastard JP, Robert JJ, Jardel C, Bruckert E, Grimaldi A, Hainque B. Is quantitative insulin sensitivity check index, a fair insulin sensitivity index in humans? *Diabetes Metab* 2001;27:69–70. [PubMed: 11240450]
46. Hrebicek J, Janout V, Malincikova J, Horakova D, Cizek L. Detection of insulin resistance by simple quantitative insulin sensitivity check index QUICKI for epidemiological assessment and prevention. *J Clin Endocrinol Metab* 2002;87:144–147. [PubMed: 11788638]
47. Sterling RK, Lissen E, Clumeck N, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. *Hepatology* 2006;43:1317–1325. [PubMed: 16729309]
48. Shire, N.; Rao, MB.; Anderson, JA., et al. Improving non-invasive discrimination of fibrosis stage in HIV/HCV co-infected patients. Poster presented at: 14th Conference on Retroviruses and Opportunistic Infections (CROI 2007); February 28, 2007; Los Angeles, CA. Available from: <http://www.retroconference.org/2007/PDFs/914.pdf>
49. World Health Organization (1997). Report of a WHO Consultation presented at the World Health Organization. Geneva, Switzerland: Publication WHO/NUT/NCD/98.1. World Health Organization; 1997 Jun 3–5. Obesity: Preventing and managing the global epidemic.
50. Jones CY, Wilson IB, Greenberg AS, et al. Insulin resistance in HIV-infected men and women in the nutrition for healthy living cohort. *J Acquir Immune Defic Syndr* 2005;40:202–211. [PubMed: 16186739]
51. Brown TT, Li X, Cole SR, Kingsley LA, et al. Cumulative exposure to nucleoside analogue reverse transcriptase inhibitors is associated with insulin resistance markers in the Multicenter AIDS Cohort Study. *AIDS* 2005;19:1375–1383. [PubMed: 16103768]
52. El-Sadr WM, Mullin CM, Carr A, et al. *HIV Med* 2005;6:114–121. [PubMed: 15807717]
53. Soriano V, Puoti M, Garcia-Gasco P, et al. Antiretroviral drugs and liver injury *AIDS* 2008;22:1–13.
54. Delgado-Borego A, Casson D, Schoenfeld D, et al. Hepatitis virus is independently associated with increased insulin resistance after liver transplantation. *Transplantation* 2004;77:703–710. [PubMed: 15021833]
55. Merchante N, Macias J, Ramayo E, et al. Insulin resistance is not associated with liver fibrosis progression in HIV/hepatitis C-virus coinfecting patients. *J Viral Hepat* 2006;13:449–456. [PubMed: 16792538]
56. Su AI, Pezacki JP, Wodicka L, et al. Genomic analysis of the host response to hepatitis C virus infection. *Proc Natl Acad Sci USA* 2002;99:15669–15674. [PubMed: 12441396]
57. Walli R, Hertfort O, Michl GM, et al. Treatment with protease inhibitors associated with peripheral insulin resistance and impaired glucose tolerance in HIV-1 infected patients. *AIDS* 1998;12(15):F167–F173. [PubMed: 9814858]
58. Noor M, Lo J, Mulligan, et al. Metabolic effects of indinavir in healthy HIV-seronegative men. *AIDS* 2001;15:F11–F18. [PubMed: 11399973]
59. Lo JC, Kazemi MR, Hsue PY, et al. The relationship between nucleoside analogue treatment duration, insulin resistance, and fasting arterialized lactate level in patients with HIV infection. *Clin Infect Dis* 2005;41:1335–1340. [PubMed: 16206112]
60. Blumer RME, van Vonderen MGA, Sutinen J, et al. Zidovudine/ lamivudine contributes to insulin resistance within 3 months of starting combination antiretroviral therapy. *AIDS* 2008;22:227–236. [PubMed: 18097225]
61. Meininger G, Hadigan C, Rietschel P, Grinspoon S. Body composition measurements as predictors of glucose and insulin abnormalities in HIV positive men. *Am J Clin Nutr* 2002;76:460–465. [PubMed: 12145023]
62. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985;28:412–419. [PubMed: 3899825]

Table 1

Subject characteristics stratified by HIV/HCV infection status

Characteristic	HIV mono-infected (N = 76)	HCV mono-infected (N = 62)	HIV/HCV co-infected (N = 97)	Uninfected control (N = 98)	P value ^a
Age (y)	40 ± 9	38 ± 9	42 ± 7	36 ± 11	<0.0001
Male	42 (55)	55 (89)	81 (84)	51 (52)	<0.0001
Current smoker	35 (46)	58 (94)	69 (71)	60 (61)	<0.0001
Current drinker	33 (43)	37 (60)	32 (33)	57 (58)	0.0008
Drug use	13 (17)	55 (89)	48 (49)	46 (47)	NA ^b
Body mass index (kg/m ²)	28.2 ± 7.2	26.7 ± 4.8	26.6 ± 4.0	29.5 ± 6.0	0.0010
Central obesity ^c	17/53 (32)	5/39 (13)	11/62 (18)	8/22 (36)	0.049
Triglycerides (mmol/L) ^d	1.7 (1.1, 2.4)	0.95 (0.77, 1.3)	1.4 (0.89, 2.5)	1.0 (0.67, 1.8)	<0.0001
Insulin (pmol/L) ^d	68 (42, 125)	63 (45, 97)	92 (58, 144)	72 (49, 104)	0.030
Glucose (mmol/L) ^d	4.8 (4.4, 5.2)	4.9 (4.3, 5.3)	4.8 (4.3, 5.3)	4.7 (4.4, 5.2)	0.28
QUICKI	0.34 ± 0.04	0.34 ± 0.04	0.33 ± 0.04	0.34 ± 0.04	0.025
QUICKI <= 0.35 ^e	42 (55)	34 (55)	67 (69)	61 (62)	0.19
HOMA ^d	2.02 (1.25, 4.22)	1.92 (1.31, 2.88)	2.89 (1.66, 4.60)	2.16 (1.37, 3.44)	0.02
FIB-4 ^{d,f}	0.97 (0.68, 1.2)	1.1 (0.68, 1.7)	1.5 (1.2, 2.8)	0.71 (0.50, 0.85)	<0.0001
FIB-4 >3.25 ^{f,g}	0/74 (0)	3/62 (5)	16/95 (17)	0/42 (0)	<0.0001
Years with HCV ^d	NA	12 (6, 22)	23 (17, 30)	NA	<0.0001
Years with HIV ^d	8 (5, 12)	NA	11 (8, 14)	NA	0.0005
CD4 count (cells/mm ³)	448 ± 283	NA	387 ± 253	NA	0.14
Viral load (log ₁₀ copies/mL)	3.2 ± 1.1	NA	3.3 ± 1.1	NA	0.66
Antiretroviral therapy	58 (76)	NA	66 (68)	NA	0.23

Data are shown as mean ± SD or number (percent)

^aP values based on F test for continuous variables, Chi-square or Fisher's exact test for categorical variables.

^bNA: Not applicable - Difference in drug use among groups is based on recruitment strategy.

^cCentral obesity was defined as a waist circumference of > 102 cm in men and >88 cm in women

^dMedian (25th, 75th percentile).

^eValues of QUICKI below 0.35 are associated with insulin resistance

^fBased on N = 253 (74, 42, 95, 42, respectively)

^gFIB-4 values >3.25 are associated with significant fibrosis

HIV: human immunodeficiency virus infection, HCV: hepatitis C virus infection, QUICKI: Quantitative Insulin Sensitivity Check Index, HOMA: Homeostatic Model Assessment, FIB-4 score to assess liver injury

Table 2Univariate predictors of QUICKI in 333 study participants ^a

Characteristic	Correlation coefficient, r	Between-group difference in QUICKI±SE	P value
Age (y)	-0.11	--	0.049
Male	--	-0.00086 ± 0.005	0.85
Current smoker	--	0.0035 ± 0.004	0.42
Current drinker	--	0.0083 ± 0.004	0.048
Drug user	--	0.0065 ± 0.004	0.12
Body mass index (kg/m ²)	-0.33	--	<0.0001
Triglycerides (mmol/L)	-0.27	--	<0.0001
HIV infection	--	-0.0095 ± 0.004	0.024
HCV infection	--	-0.0078 ± 0.004	0.065
Years with HCV	-0.12	--	0.14
FIB-4 ^b	-0.20	--	0.0017
<u>HIV-infected only</u>	--	--	--
Years with HIV	-0.15	--	0.05
CD4 count (cells/mm ³)	0.11	--	0.10
Viral load (log ₁₀ copies/mL)	0.068	--	0.38
Antiretroviral therapy	--	-0.0048 ± 0.0066	0.47

^aUnivariate associations between QUICKI values and independent variables of interest were determined using Pearson's coefficient of correlation for continuous, normally distributed and log transformed variables or the independent groups *t*-test for categorical variables. HCV: hepatitis C virus infection, FIB-4 score to assess liver injury, HIV: human immunodeficiency virus infection. Lower values of QUICKI are indicative of greater insulin resistance. Thus, variables negatively associated with QUICKI are associated with insulin resistance.

^bBased on N=253.

Table 3

Multivariate analyses: predictors of QUICKI stratified by HIV/HCV infection status

Characteristic	HIV mono-infected N=76	HCV mono-infected N=62	HIV/HCV co-infected N=97	Uninfected control N=98
	Estimated effect on QUICKI ± SE	Estimated effect on QUICKI ± SE	Estimated effect on QUICKI ± SE	Estimated effect on QUICKI ± SE
Age (years)	-0.00073 ± 0.00057	-0.00069 ± 0.00056	-0.00018 ± 0.00057	0.00025 ± 0.00031
Male	0.012 ± 0.010	0.0078 ± 0.015	-0.017 ± 0.011	-0.0040 ± 0.0073
Body mass index (kg/m ²)	-0.0018 ± 0.00071 [†]	-0.0036 ± 0.0010 [‡]	-0.0029 ± 0.00093 [‡]	-0.0018 ± 0.00059 [‡]
Triglycerides (mmol/L)	-0.86 ± 0.64	-0.24 ± 0.82	-0.88 ± 0.48	-1.83 ± 0.58 [‡]
Current drinker	0.0050 ± 0.0095	-0.0077 ± 0.0097	0.0015 ± 0.0079	0.015 ± 0.0069 [†]
Years with HIV	-0.00047 ± 0.0011	NA	0.00032 ± 0.00084	NA
CD4 count (cells/mm ³)	0.000026 ± 0.000019	NA	-0.000024 ± 0.000018	NA
Viral load (log ₁₀ copies/mL)	0.0065 ± 0.0058	NA	0.0061 ± 0.0048	NA
Antiretroviral therapy	0.0094 ± 0.014	NA	-0.021 ± 0.011 [†]	NA

HIV: human immunodeficiency virus infection, HCV: hepatitis C virus infection, NA, not applicable. Triglyceride levels were transformed using the natural log (ln) for analysis. Lower values of QUICKI are indicative of greater insulin resistance. Thus, variables negatively associated with QUICKI are associated with insulin resistance.

[†] P≤0.05

[‡] P≤0.01

Table 4Effect of HCV infection as a predictor of QUICKI ^a

Characteristic	HIV-infected (N = 173)	HIV-uninfected (N = 160)
	Estimated effect on QUICKI ± SE	Estimated effect on QUICKI ± SE
HCV infection	-0.015 ± 0.0061 [†]	-0.0071 ± 0.0063
Age (years)	-0.00057 ± 0.00038	-0.000027 ± 0.00029
Male	0.0022 ± 0.0069	-0.0026 ± 0.0071
Body mass index (kg/m ²)	-0.0024 ± 0.00054 [‡]	-0.0025 ± 0.00054 [‡]
Triglycerides (mmol/L)	-0.85 ± 0.39 [†]	-1.24 ± 0.49 [†]
Current drinker	0.0042 ± 0.0059	0.0066 ± 0.0059
Years with HIV	-0.00016 ± 0.00065	NA
CD4 count (cells/mm ³)	0.0000044 ± 0.000013	NA
Viral load (log ₁₀ copies/mL)	0.0011 ± 0.0037	NA
Antiretroviral therapy	-0.0038 ± 0.0083	NA

^a HIV: human immunodeficiency virus infection, HCV: hepatitis C virus infection, NA, not applicable. Triglyceride levels were transformed using the natural log (ln) for analysis. Lower values of QUICKI are indicative of more insulin resistance. Thus, variables negatively associated with QUICKI are associated with insulin resistance.

[†] P ≤ 0.05,

[‡] P ≤ 0.01

Table 5Effect of FIB-4 as a predictor of QUICKI ^a

Characteristic	Model without FIB-4	Model with FIB-4
	Estimated effect on QUICKI ± SE	Estimated effect on QUICKI ± SE
HCV infection	-0.012 ± 0.0046 [‡]	-0.0092 ± 0.0047 [‡]
FIB-4	---	-0.0035 ± 0.0016 [‡]
HIV	-0.0080 ± 0.065	-0.0067 ± 0.0064
Age (years)	-0.00046 ± 0.00025	-0.00029 ± 0.00025
Male	0.0019 ± 0.0052	-0.0017 ± 0.0052
Body mass index (kg/m ²)	-0.0025 ± 0.00039 [‡]	-0.0025 ± 0.00038 [‡]
Triglycerides (mmol/L)	-0.83 ± 0.31 [‡]	-0.89 ± 0.31 [‡]
Current drinker	0.0049 ± 0.0059	0.0048 ± 0.0043
NRTI +NNRTI	-0.0059 ± 0.0064	-0.0061 ± 0.0064
PI	-0.0037 ± 0.0059	-0.0023 ± 0.0059

^a HIV: human immunodeficiency virus infection, HCV: hepatitis C virus infection, NA, not applicable. Triglyceride levels were transformed using the natural log (ln) for analysis. Lower values of QUICKI are indicative of more insulin resistance. Thus, variables negatively associated with QUICKI are associated with insulin resistance.

[‡] P≤0.05

[‡] P≤0.01