

Hepatitis C

Insulin Resistance and Diabetes

Research continues to accumulate linking hepatitis C virus infection with blood glucose abnormalities such as insulin resistance and diabetes, as shown in several recently published studies.

As described in the first report, published in the September 2007 *Journal of Viral Hepatitis*, M. Yoneda and colleagues designed a study to test the hypothesis that HCV infection may promote insulin resistance. The researchers prospectively evaluated 47 participants with chronic hepatitis C who underwent liver biopsy; obese patients and those with pre-existing type 2 diabetes or a history of heavy alcohol consump-

tion were excluded. Non-diabetic individuals without hepatitis C served as controls. Although fasting blood glucose levels were within the normal range for all patients, a univariate analysis revealed a significant correlation between HCV viral load and insulin resistance determined using modified homeostasis model of insulin resistance (HOMA-IR) scores. In the hepatitis C patients, there was no association between the amount of visceral fat and HOMA-IR scores, but these factors were significantly related in people without hepatitis C or diabetes. This remained the case after adjusting for factors such as age and sex. These findings led the researchers to conclude that, "HCV is directly

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Executive Director
Editor-in-Chief,
HCSP Publications
Alan Franciscus

Contributor:
Liz Highleyman

Managing Editor, Webmaster
C.D. Mazoff, PhD

Design/Production
Alan Franciscus

Contact Information:
The Hepatitis C Support Project
PO Box 427037
San Francisco, CA 94142

www.hcvadvocate.org

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associated with insulin resistance in a dose-dependent manner, independent of the visceral adipose tissue area.”

In the second study, reported in the October 2007 *American Journal of Gastroenterology*, A. Lecube and colleagues investigated whether impaired fasting glucose and type 2 diabetes influence response to interferon-based therapy for hepatitis C. The study included 178 previously untreated participants with chronic HCV infection who received combination therapy with interferon plus ribavirin. The 67 patients who achieved sustained virological response (SVR) after completing treatment had lower plasma glucose levels and were less likely to have blood glucose abnormalities than the 111 nonresponders (44% vs 24%). Participants with normal blood glucose had an SVR rate of 45%, compared with 28% for those with impaired fasting glucose and just 16% among those with type 2 diabetes. After controlling for other factors, glucose abnormalities were independently associated

with lack of sustained response. The researchers concluded that, “Glucose abnormalities are an independent predictor of poor virological response to combined therapy in hepatitis C virus infected patients.”

Insulin resistance also predicts more severe liver fibrosis in people with either chronic hepatitis C or non-alcoholic fatty liver disease (NAFLD), according to a study published in the September 2007 issue of *Gut*. G. Svegliati-Baroni and colleagues assessed the relative contributions to fibrosis of liver steatosis (fat accumulation), metabolic abnormalities, and insulin resistance measured by different parameters in 90 patients with chronic hepatitis C and 90 matched subjects with NAFLD. The prevalence of basal insulin resistance (defined as a HOMA-IR score above the 75th percentile of normal) was 23% in the hepatitis C patients and 58% in those with NAFLD. When assessed using post-load insulin resistance (defined as an oral glucose insulin sensitivity index score below the 25th percentile), the corresponding fig-

ures increased to 29% and 68%. After adjusting for age, sex, and body mass index (BMI), the oral glucose insulin sensitivity score was an independent predictor of severe fibrosis in both hepatitis C and NAFLD patients, regardless of steatosis. Further, the researchers found that the oral glucose insulin sensitivity index was a more sensitive and specific test than HOMA-IR for identifying patients with severe fibrosis.

Finally, as reported in the September 2007 *American Journal of Gastroenterology*, T. Komura and colleagues looked at the relationship between diabetes and recurrence of hepatocellular carcinoma (HCC) after surgery. While most experts agree that diabetes is a risk factor for the initial development of HCC, less is known about the influence of diabetes on post-operative HCC recurrence. The study included 90 participants who had undergone resection surgery to remove liver tumors. Survival after surgery was assessed in two groups of patients, those with

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and without diabetes. A Kaplan-Meier survival analysis showed that both recurrence-free and overall survival rates were significantly lower among the diabetic patients. This association was even more clear when the investigators restricted their analysis to the subgroup of patients with hepatitis C. The researchers concluded that, “diabetes is a risk factor for the recurrence of HCV-related HCC and decreases the overall survival rates after surgical treatment.” Based on these findings, they recommended that diabetic hepatitis C patients with HCC should be closely followed for postoperative cancer recurrence.

Monitoring HIV Disease Progression in People with Cirrhosis

Absolute CD4 T-cell count is usually used to monitor immune function in people with HIV. Recently, it was shown that HIV negative individuals with liver cirrhosis had abnormally low CD4 cell counts, but normal CD4 cell per-

centages (the proportion of all lymphocytes that carry the CD4 marker), suggesting that CD4 percentage might be a more accurate marker of disease progression in HIV positive patients with cirrhosis. As reported in the September 1, 2007 issue of *Clinical Infectious Diseases* (and also at the International AIDS Society conference in July), M. Bongiovanni and colleagues looked at absolute CD4 cell counts and CD4 percentages in about 6,000 HIV positive participants in the Italian Cohort of Antiretroviral-Naive Patients, of whom 38% were coinfecting with HCV and 5% with HBV. About 3% had cirrhosis at enrollment and an additional 1% developed cirrhosis during the follow-up period. Among patients with cirrhosis, a higher CD4 cell count^{3/4}but not a higher CD4 percentage^{3/4}was associated with a lower risk of progression to AIDS. Among non-cirrhotic patients (with or without HBV or HCV), both lower absolute CD4 cell count and lower CD4 percentage predicted progression to AIDS. After controlling

for both CD4 values, people with cirrhosis were significantly more likely to develop an AIDS-defining illness. The researchers concluded that for patients with cirrhosis, “CD4 cell count seemed to be better predictor of the risk of developing an AIDS-defining illness than the CD4 cell percentage,” and therefore should be used to guide decisions about HIV treatment regardless of liver disease status.

