

Correspondence

Re: The Relationship of Hepatitis Antibodies and Elevated Liver Enzymes with Impaired Fasting Glucose and Undiagnosed Diabetes

To the Editor: I enjoyed reading your article about elevated liver enzymes and undiagnosed diabetes.¹ In the literature there have been several hypotheses to explain the correlation of hepatitis and diabetes type 2. One hypothesis is that the more advanced the liver fibrosis, the higher the risk for diabetes due to impaired glucogenesis by the liver.² More recent studies show that in particular hepatitis C (HCV) may interfere with insulin receptor substrate 1 and 2 through increased levels of proinflammatory cytokines.³ This hypothesis of HCV and diabetes has not been consistently demonstrated in clinical trials. In post-treatment longitudinal trials, those with a history of HCV who develop diabetes mellitus (DM) also have other risk factors such as increased age, increased body mass index (BMI), and family history of DM; these are all individual predictors of insulin resistance, which distorts this hypothesis of whether HCV can be directly implicated in the development of diabetes type 2.⁴ In people with fatty liver disease without hepatitis C, we have seen as well that increased age, BMI, and family history of DM are all individual predictors of insulin resistance and prediabetes.⁵

In your article you state that increased alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) could be considered a precursor to prediabetes, but given what we know about liver steatosis and insulin

resistance, I cannot help but wonder whether increased ALT and GGT is rather just a symptom of steatosis caused by insulin resistance.

Paula P. Cox-North, MN
University of Washington
Seattle, Washington
paulac@u.washington.edu

References

1. Mainous AG, Diaz VA, King DE, Everett CJ, Player MS. The relationship of hepatitis antibodies and elevated liver enzymes with impaired fasting glucose and undiagnosed diabetes. *J Am Board Fam Med* 2008;21(6):497–503.
2. 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;133:592–9.
3. Kawaguchi T, Yoshida T, Harada M, et al. Irs downregulates insulin receptor substrates 1 and 2 through upregulation of suppressor of cytokine signaling 3. *Am J Pathol* 2004;165:1499–1508.
4. Giordinino C, Bugianesi E, Smedile A, et al. Incidence of type 2 diabetes mellitus and glucose abnormalities in patients with chronic hepatitis C infection by response to treatment: results of a cohort study. *Am J Gastroenterol* 2008;103:2481–7.
5. Clark JM. Epidemiology of non alcoholic fatty liver disease in adults. *J Clin Gastroenterol* 2006;40:S5–S10.

doi: 10.3122/jabfm.2009.03.080247

Dr. Mainous declined to respond to this letter.