

**ORIGINAL RESEARCH**

Fatty liver disease in type 2 diabetes: Common and often unmanaged

This study of patients with type 2 diabetes in a large rural clinic showed that abnormal liver function tests do not usually lead to diagnostic imaging studies.

Eric L. Johnson, MD
Department of Family and
Community Medicine,
University of North Dakota
School of Medicine and Health
Sciences and Altru Health
System Diabetes Center,
Grand Forks, ND

Eric.l.johnson@med.und.edu

*The author reported that he
has served on Novo Nordisk's
speakers' bureau.*

ABSTRACT

Purpose ▶ The objective of this pilot study was to evaluate the prevalence and management of nonalcoholic fatty liver disease in a rural type 2 diabetes population.

Methods ▶ We randomly selected 100 patients with type 2 diabetes from a large rural clinic/hospital system in the upper Midwest and conducted a chart review to determine the prevalence of abnormal results of serum liver function tests and liver imaging (eg, computed tomography, ultrasound, magnetic resonance imaging). We also determined the number of patients who were given a diagnosis of fatty liver disease and who among those were subsequently managed for the condition.

Results ▶ Of the 100 subjects, 40 had abnormal serum liver function testing, and half of those individuals underwent imaging. This resulted in a diagnosis of fatty liver disease in 11 (27.5% of the 40 with abnormal liver function). Only 4 patients received specific interventions for fatty liver disease.

Conclusion ▶ In this rural population, fatty liver disease was common and untreated, suggesting a possible need for a change in screening and management protocols.

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the United States.¹ In particular, NAFLD and the related

inflammatory nonalcoholic steatohepatitis (NASH) often develop in individuals who are obese or who have prediabetes or type 2 diabetes, affecting up to 75% of patients with these conditions.²

In addition to NAFLD and NASH, other liver diseases associated with type 2 diabetes include cirrhosis, hepatocellular carcinoma, liver failure, and hepatitis.^{1,3,4} Of patients with type 2 diabetes, more than 600,000 have cirrhosis; 4.4% of diabetes-related deaths have been attributed to cirrhosis.^{4,5}

NAFLD and NASH share a common pathophysiology in type 2 diabetes with respect to insulin resistance, which results in hyperlipidemias that enhance fatty deposits in the liver.^{1,2} Hepatic fat accumulation is also associated with increasing measures of inflammation, including C-reactive protein.⁶

Resultant liver function test abnormalities and characteristic appearance on imaging studies (ultrasound, computed tomography [CT], or magnetic resonance imaging [MRI]) may be similar in NAFLD and NASH.¹⁻³ Liver biopsy therefore is necessary to distinguish NAFLD from NASH, with NASH showing characteristic inflammatory and fibrotic changes.^{1,2} Evaluations of patients with minor liver test abnormalities reveal that up to 98% may have liver disease, most often fatty liver disease.⁷

Weight loss is a strategy for managing NAFLD and NASH, although large random-

➤ **Of 40 patients with abnormal serum liver function tests, only 10 were specifically referred for imaging studies that might confirm a diagnosis of fatty liver disease.**

ized controlled trials are lacking.⁸⁻¹⁰ Several agents used for diabetes and dyslipidemias, including glucagon-like peptide-1 (GLP-1) mimetics, metformin, thiazolidinediones, and statins, have been studied as possible treatments for NAFLD and NASH.⁸⁻¹³ Currently, these medications carry cautions or warnings about using them in patients with liver disease and are not indicated as treatments for NAFLD or NASH.

SUBJECTS AND METHODS

One hundred patients were randomly selected from a type 2 diabetes patient database at the Altru Health System (Grand Forks, ND) for cross-sectional analysis. Manual data extraction from “paper charts” was necessary in some cases, limiting the size of the study.

All subjects had a diagnosis of type 2 diabetes confirmed by American Diabetes Association criteria, were between the ages of 18 and 64 years, and had no known liver disease other than that associated with their diabetes. Other criteria included visiting a health care provider regarding diabetes management within the last year and having undergone laboratory blood testing of liver function within the last 5 years. The study population comprised an equal number of men and women.

We collected data about abnormal liver function from blood test results, including levels of aspartate transaminase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP); results of radiologic imaging of the liver (ultrasound, MRI, or CT) and liver biopsy; any interventions (medication changes, lifestyle management, or surgery); and referral to a specialist (gastroenterologist or surgeon).

DATA ANALYSIS

Of the 100 subjects, 40 had at least one abnormal serum liver function test (AST, ALT, or ALP), although we could find no record of tests for one of the 100 subjects. Of the 40 with abnormal test results, 17 (42.5%) were women and 23 (57.5%) were men. None of these patients had highly elevated levels of AST, ALT, or ALP.

Of the 40 patients with abnormal serum liver function tests, only 10 (25%) were specifically referred for imaging studies related to a possible diagnosis of fatty liver disease. Four of these 10 patients (1 woman and 3 men) had both ultrasound and CT imaging. Another 10 subjects (25%) had incidental findings of fatty liver disease on imaging performed for another presumed diagnosis or symptom, eg, abdominal pain. Overall, 11 (6 men, 5 women) of the 40 subjects (27.5%) with at least one abnormal liver function test received a diagnosis of fatty liver disease based on imaging findings. None of the subjects had a diagnosis of cirrhosis or other end-stage liver disease.

A medical intervention was offered to 4 of the 11 patients (2 women and 2 men) who received a diagnosis of fatty liver disease. Practitioners specifically referred one woman for medical weight loss management and another for weight loss surgery. One man was advised to stop taking metformin, and another was referred to a dietician for lifestyle weight loss management. No patient was referred to a gastroenterologist or any other specialist for further evaluation or biopsy.

DISCUSSION

Although a small sample size limits the strength of this pilot study, the finding that fatty liver disease is common in patients with type 2 diabetes in a rural community hospital population supports other published data. As only half of the subjects with abnormal liver function tests had imaging studies, it's likely that some patients in the study group who did not undergo imaging also had NAFLD, NASH, or other liver disease, but it was not diagnosed.

■ **While no specific screening guidelines** for fatty liver disease in patients with type 2 diabetes have been issued, clinical interest in this area has been growing, and this study suggests some avenues for further exploration.³ In the institution where this study was conducted, it appears that liver function tests were most likely to be performed in conjunction with routine monitoring of the use of statins, metformin, or other medications or because of a symptom such as abdominal pain. Yet given the widespread availability

and relatively low cost of such tests, periodic monitoring of serum liver function in patients with type 2 diabetes may be warranted.¹⁴

Patients found to have persistent or recurrent abnormal liver function tests could then be referred for further evaluation with ultrasound, CT, or MRI.¹⁴ Ultrasound has the benefit of lower cost and avoidance of intravenous contrast, which may be important for patients with renal dysfunction.¹⁴ Based on

the results of these tests, appropriate medical interventions could then follow. **JFP**

CORRESPONDENCE

Eric L. Johnson, MD, 501 N. Columbia Road, Stop 9037, Grand Forks, ND 58202; eric.l.johnson@med.und.edu

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The high prevalence of fatty liver disease in this population of patients with type 2 diabetes supports earlier findings.