



Some People With Dementia May Have Undiagnosed Liver Disease

About 5% of veterans with dementia had evidence of liver cirrhosis, which can lead to cognitive impairment.

February 5, 2024 By Liz Highleyman

Some people with apparent dementia may actually have hepatic encephalopathy, a potentially treatable cause of cognitive impairment associated with advanced cirrhosis, according to study findings reported in [JAMA Network Open](#). Simple noninvasive measures can help determine which patients warrant further follow-up for liver disease.

“The findings of this study suggest that clinicians treating patients with dementia should investigate a reversible factor associated with cognitive decline, including missed or undiagnosed cirrhosis with hepatic encephalopathy,” wrote Jasmohan S. Bajaj, MD, of Virginia Commonwealth University and the Richmond Veterans Affairs Medical Center, and colleagues.

The liver has [many vital functions](#), including regulating metabolism, storing nutrients and filtering toxins. Over time, chronic [hepatitis B](#) or [hepatitis C](#), [fatty liver disease](#), heavy alcohol consumption and other causes of liver injury can lead to the buildup of scar tissue (fibrosis), [cirrhosis](#) and [liver cancer](#).

Liver damage is often asymptomatic at early stages, but if left untreated, it can progress to decompensated cirrhosis, meaning the organ can no longer do its job. One outcome of liver failure is hepatic encephalopathy, which occurs when the buildup of ammonia and other toxic substances affect the brain, leading to cognitive dysfunction, disorientation, mood changes and, ultimately, coma. Hepatic encephalopathy may be reversible if diagnosed and treated promptly.

Bajaj and colleagues from other VA medical centers across the United States asked whether some patients with dementia might have undiagnosed cirrhosis and possibly treatable cognitive impairment. They noted that dementia and hepatic encephalopathy “are challenging to distinguish clinically,” and undiagnosed liver disease could lead to missed treatment opportunities.

Using data from the Veterans Health Administration (VHA), the study authors conducted a retrospective analysis of 177,422 veterans with a diagnosis of dementia at two or more clinic visits. Findings from the main cohort were validated with a more extensive analysis of two cohorts

from the Richmond VA Medical Center.

In the nationwide VHA cohort, the median age was about 78 years. As is typical of an older veteran population, 97% were men, and about 80% were white. The participants had no prior diagnosis of cirrhosis, but they had enough available lab test data to calculate a [FIB-4 score](#). This biomarker index, used to estimate the extent of fibrosis, incorporates age, ALT and AST liver enzyme levels and platelet count.

The researchers found that 10.3% of the patients in the main VHA cohort had a FIB-4 score greater than 2.67, suggesting advanced fibrosis, while 5.3% had a score above 3.25, suggesting cirrhosis. The proportions were similar in a validation cohort of 80 patients with dementia seen in the Richmond VA's geriatrics clinic (11.2% and 4.4%, respectively). In another validation cohort of 89 patients with dementia and a high FIB-4 score, a majority had other evidence of advanced liver disease in their medical records, including liver stiffness measurements and imaging.

After adjusting for other factors, high FIB-4 scores were significantly associated with older age, viral hepatitis (79% higher risk), alcohol use disorder (56% higher risk), congestive heart failure and chronic kidney disease. Conversely, white individuals, rural residents, tobacco users and people with diabetes, elevated blood lipids or stroke were less likely to have high scores. While hepatitis C virus and alcohol use were expectedly associated with high FIB-4 scores, the inverse association with metabolic and other comorbidities was not expected based on prior studies.

"The findings of this cohort study suggest that clinicians encountering patients with dementia should be encouraged to screen for cirrhosis using the FIB-4 score to uncover reversible factors associated with cognitive impairment, such as hepatic encephalopathy, to enhance outcomes," the study authors concluded.

"These findings highlight the potential to enhance cognitive function and quality of life by increasing awareness of risk factors and diagnostic indicators of advanced liver disease that may be associated with hepatic encephalopathy as a factor or as a differential diagnosis of dementia among clinicians other than liver specialists," they wrote. "While alcohol use disorder and viral hepatitis are well known to be associated with advanced liver disease, these findings should encourage health care professionals taking care of patients with dementia, including primary care, urgent care clinicians, geriatricians and neurologists, to seek these out and diagnose cirrhosis as a potential factor associated with cognitive dysfunction."

"The disparity in potential undiagnosed cirrhosis in veterans with dementia who lived in urban areas, were of Hispanic ethnicity and were not white is an important issue," they added.

"Dementia disproportionately affects Black and Hispanic veterans and is diagnosed later in the disease course in these populations, which has been attributed to lack of high-quality health care access for minoritized populations. A lack of access to health care services could also explain potentially underdiagnosed cirrhosis, which reiterates the need for focus on these subpopulations to accurately diagnose cirrhosis and potentially hepatic encephalopathy."

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