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## Researching the Overlap: Hepatic Encephalopathy and Dementia in Focus

### Dr. Turck:

This is *NeuroFrontiers* on ReachMD, and I'm Dr. Charles Turck. Joining me to share findings from two studies examining a potential cause and reversal of hepatic encephalopathy in patients with dementia is primary investigator Dr. Jasmohan Bajaj. He's a tenured Professor of Medicine in the Division of Gastroenterology, Hepatology, and Nutrition at Virginia Commonwealth University with a joint appointment at the Richmond VA Medical Center. Dr. Bajaj, welcome to the program.

### Dr. Bajaj:

Thank you so much for having me, and I'm so excited to be here.

### Dr. Turck:

Well, to start us off, would you give us a broad overview of hepatic encephalopathy and what led you to study it in the context of dementia?

### Dr. Bajaj:

Well, thank you. A very important problem that we have currently is aging of the population and also diabetes, obesity, and alcohol use. A lot of these conspire together to cause injury of the liver, which in the end stage is known as cirrhosis. Around 50 percent of people with cirrhosis have what we call "hepatic encephalopathy," which means some kind of brain dysfunction, either subclinical or overt, which we call "clinical hepatic encephalopathy" in those patients. The unfortunate part is that the cirrhosis has a long phase in which there's absolutely no symptoms, so a lot of patients who have diabetes, obesity, alcohol, or viral hepatitis could actually be undiagnosed with cirrhosis for a very long time. And a lot of the issues that people with dementia face and those with hepatic encephalopathy can have similar symptoms.

I as a gastroenterologist and hepatologist have spent almost my entire life studying hepatic encephalopathy, and as patients with cirrhosis are growing older, we find it harder and harder to differentiate between what is hepatic encephalopathy and what is dementia and what could be both in this patient population. This is important to study because one population is reversible, which is hepatic encephalopathy, or easily treatable; whereas, of course, as you know, dementia is incredibly hard to treat once it has settled in. So therefore, the overlap between hepatic encephalopathy or dementia and the presence of potentially undiagnosed cirrhosis and HE in people with dementia was a big concern for us and potentially for a lot of your readers and your listeners.

### Dr. Turck:

So with that background in mind, let's jump into the studies you conducted. Would you tell us about their respective designs?

### Dr. Bajaj:

Yes, thank you for that. There are two studies: one published in *The American Journal of Medicine*, and another one published in *JAMA Network Open*. As you mentioned in my introduction, I have a joint appointment with the Veterans Medical Center as well as the university. So the first study in *JAMA Network Open* that was published in January 2024 actually took veterans with dementia that were diagnosed across the national VA databases. In addition to that, we also did a review of the charts locally in the Richmond VA, not only for the people who had dementia but also for people who were actually actively seen in clinic to see how many of them had potentially undiagnosed cirrhosis. So there is a way to screen for cirrhosis using easily available blood tests called the fibrosis 4, or the FIB-4 index.

This is usually applied using multiple population-based studies, and it involves the two blood evaluations of platelet count, AST and ALT, which are liver markers, as well as the age. So we used the cutoff of FIB-4 to figure out how many people who had dementia could have had potential cirrhosis underlying. So what we need to do and what we did in the larger study is we found out that around 5–10 percent of people with dementia who had no diagnosis of cirrhosis in the VA population could have had undiagnosed cirrhosis, and we confirmed that in the chart review done locally as well as in the people who had dementia that were actively seen in our clinic.

Now patients who are veterans are a little bit different than people who are seen in the non-veteran clinics. People who are veterans are much more likely to be older, much more likely to be men, and much more likely to be in a situation where there are less minorities, so what we wanted to study in *The American Journal of Medicine* paper was whether these similar findings could also be found in a non-veteran national cohort, and we used this database called the TriNetX. This involves multiple people around the country with ensured nonveteran visits. And we used the identical criteria that we had used for the VA study in this, and what we found to our surprise that it was actually 13 percent instead of 10 percent. Thirteen percent of these patients had potential for undiagnosed cirrhosis, and therefore, even if some of them had hepatic encephalopathy, that means we actually missed a lot of this. So what we found, to make a long story short, the veterans and in the non-veterans cohort with dementia in patients who did not have diagnosed cirrhosis, the rate of potential undiagnosed cirrhosis and hepatic encephalopathy could be as high as 10–13 percent, which gave us great pause.

**Dr. Turck:**

For those just tuning in, you're listening to *NeuroFrontiers* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Jasmohan Bajaj about his research focusing on hepatic encephalopathy in patients with dementia.

So given the findings you just shared with us, Dr. Bajaj, what can you tell us about their significance and implications?

**Dr. Bajaj:**

So the implications are quite huge because as I said, cirrhosis is often undiagnosed because it does not cause symptoms until it's too late. So what are the consequences of missing cirrhosis in general? And specifically in people with dementia? In general, patients with cirrhosis have a high chance of progressing to developing cancer of the liver; they have a high chance of developing complications, such as hepatic encephalopathy that we talked about, which is a brain dysfunction; they have chances of getting bleeding or swelling of their belly as a result of the cirrhosis and the liver failure; and they can obviously get jaundiced and get infections because of the immunosuppression that they have. This is in general population. If you miss cirrhosis, these things might happen.

In patients with dementia, the complication of interest really is hepatic encephalopathy. So if you have dementia and you have been treated as dementia because several of the symptoms of dementia and hepatic encephalopathy can often overlap or people have contributions from both of those conditions as they grow older, then you are missing out on a chance to "reverse" some of these cognitive abnormalities because the treatment for hepatic encephalopathy is relatively easy. It's a laxative or an antibiotic that you can do, which are usually very well tolerated, and then the patients actually can come up from a coma all the way to fully functioning.

And what we actually also published in a prior smaller case series was we actually had two patients in the VA who were actually partly diagnosed with cirrhosis and one was not diagnosed at all, and they were actually considered to have dementia. However, once we treated them with medications for hepatic encephalopathy, they actually got completely better and were fully functioning members of society, so that actually gives us a little pause to figure out how many of our potential patients with dementia in which we have not investigated whether they have cirrhosis or not could potentially have a reversible cause or a treatable cause at least, such as hepatic encephalopathy. And if the results even end up being 5 percent, given the huge dementia population that we have, that is a big, big deal that we can actually really impact the patients' lives and make sure that they are able to function as fully functioning members of society.

**Dr. Turck:**

So then what other recommendations do you have to implement these findings into practice for gastroenterology and neurology specialists?

**Dr. Bajaj:**

Not only for gastroenterology and neurology, it's also important for primary care as well as people in geriatrics. The issue is for us to do everything possible in our power to ensure that we are not missing out on a reversible cause of cognitive impairment; and therefore, if a FIB-4 or something like that can actually be put into your patients' charts or you can calculate that or at least do one time an AST and ALT as well as platelet count and calculate that number, and if that number comes up to be high, then you can consider referral to a GI physician or a referral to a hepatology physician if possible so that they may assist whether this patient actually could have cirrhosis or

not, and if they have cirrhosis, whether they could be started on those medications. So it's very simple to do this test called the FIB-4, and it is very easy to actually figure out who does not have cirrhosis as a result of that.

To include cirrhosis you may need to get specialist care, but the most important thing is the eye does not see what the mind does not think of, so at this stage, awareness that cirrhosis and potentially hepatic encephalopathy could really be a differential diagnosis for dementia or an additive or a contributor to the cognitive dysfunction is really the critical take-home points of these two studies.

**Dr. Turck:**

Before we close today, Dr. Bajaj, are there any final thoughts about hepatic encephalopathy or dementia you'd like to leave with our audience?

**Dr. Bajaj:**

I would want to tell you that hepatic encephalopathy is more common than you think, and cirrhosis is even more common than you think, and you should keep a high index of suspicion for this, especially in our patient population who have obesity, diabetes, have had history or current alcohol use, or have had risk factors for viral hepatitis, which is literally everyone who is a baby boomer. So as long as we keep those guiding principles in mind and at least one time try to exclude cirrhosis in those patients or advanced liver disease, we'll be doing our patients a great service.

**Dr. Turck:**

That's a great comment for us to think on as we come to the end of today's program, and I want to thank my guest, Dr. Jasmohan Bajaj, for joining me to discuss his research focusing on the potential cause and reversal of hepatic encephalopathy in patients with dementia. Dr. Bajaj, it was great having you on the program.

**Dr. Bajaj:**

Thank you.

**Dr. Turck:**

For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.