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How to Best Manage Acute-on-Chronic Liver Failure

Dr. Buch:
In patients with cirrhosis and chronic liver disease, acute-on-chronic liver failure is emerging as a major cause of mortality. That's why an update on precipitating factors and essential management strategies is the basis of today's discussion.

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. And joining us today is Dr. Jasmohan Bajaj, Professor of Medicine at the Richmond VA Medical Center. He's also the lead author of the article "Acute-on-Chronic Liver Failure Clinical Guidelines," and this was published in the *American Journal of Gastroenterology* in February 2022.

Dr. Bajaj, welcome to the program.

Dr. Bajaj:
Thank you so much. I'm so excited to be here.

Dr. Buch:
Now, Dr. Bajaj, the definition of renal dysfunction in cirrhosis has recently been redefined. What should we know about this?

Dr. Bajaj:
So the important thing to know in cirrhosis is a little bit of creatinine goes a very long way. So if you have a creatinine that goes from 0.3 mg per deciliter increase over 24, 48 hours, this is enough for it to be called AKI, or acute kidney injury, and this has independently been associated with poor outcomes, such as death and need for liver transplant. So it is absolutely critical that we actually pay very close watch to the patients' creatinine. Because these patients already have sarcopenia, they usually run low creatinines, so even the 0.3 increase may not trigger the alarm values or the H or whatever read in your EHR might actually trigger to make you aware, so you have to actually ensure that you know what the patient's baseline creatinine was, and if it's more than 0.3 above that within 24, 48 hours, you have to actually treat that on an emergent basis. Otherwise, this may be a marker for infection. And these things, if they're not treated, can snowball into multiple organ failures and result in acute-on-chronic liver failure.

Dr. Buch:
With that definition in mind, why do you suggest thromboelastography instead of INR as a measure of coagulation risk?

Dr. Bajaj:
So the INR has its own value in prognostication of liver disease. It's a very good liver function test, but it's not really in the setting of cirrhosis a very good clotting test because there are so many other factors that go into it, the platelets and the actual clot strength and how quickly it dissolves, because patients with cirrhosis, unfortunately, are hypo- and hypercoagulable at the same time, and anything can push them into either side because they are very disbalanced. The coagulation is very disbalanced. So the TEG is one of the best ways to actually measure the whole clot formation, and it takes into account the entire cascade of clotting rather than INR, which only takes care of one aspect, which may not really be associated with a bleeding risk compared to TEG.

Dr. Buch:
Thank you. And what should we know about drug-induced liver injury as a source of acute-on-chronic liver failure?

Dr. Bajaj:
While most causes of acute-on-chronic liver failure in the United States and Western countries are related to infection, drug-induced liver injury, viral hepatitis, surgeries are also important because they are often missed and take a long time for us to put together. There are many drugs that have been known to cause drug-induced liver injury, and it all depends on whether it's how bad your liver disease

was before the drug was prescribed and how bad and what kind of pattern of liver injury that you have. For it to actually cause jaundice in liver failure, it has to be very severe, and this typically happens one month after taking the offending medications, but in some cases it can be delayed as much as 3 months, so it's important for people taking care of ACLF patients or people with cirrhosis in the hospital to have an open mind and figure out what the patient was taking, knowing that many of these medications may not really be medications at all. They may be supplements. They may be herbal things. They may be things that people take over the counter without even realizing that they are medications. So you want to make sure that at least you have an analysis of what those patients were taking, whether it was prescribed for them or not, and whether it was prescribed for a longer duration or not as well.

Dr. Buch:
Very important insight. I want to also share something personally that I teach physicians over here, and that is, lots of patients don't consider herbs or supplements to be medications. You have to ask specifically about herbs and supplements. Could you just comment on that from your perspective?

Dr. Bajaj:
Yes, absolutely. And it's all how you ask the questions. You have to ask question, "What did you take?" You don't have to say medications. You have to exactly say what you talked about: medications, especially herbal medications, Chinese herbal medications, and Ayurvedic medications. Things that people think are probiotics or supplements that are over the counter, they often do not cross the Rubicon in the patient's minds that these are actually drugs, but we have to gently disabuse them of the notion because anything you put in the mouth goes through the liver and actually can have the potential to harm your liver if not accounted for very well. Sometimes patients don't remember so the patients' companions or family members may need to be asked as well, or sometimes patients may have developed encephalopathy, sadly, so definitely we need to talk to patients' family members.

Dr. Buch:
For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Jasmohan Bajaj about acute-on-chronic liver failure.

So, Dr. Bajaj, if we zero in on our patients with cirrhosis, can you tell us why they have atypical symptoms of infection?

Dr. Bajaj:
Patients with cirrhosis, because of their immunosuppression and multiple aspects of their immune function not working very well, will often come to you with full-fledged infection without any fever. They may have what may look like listlessness, not feeling themselves, or having confusion. That may be literally the only symptoms they may have. Now when you draw their blood, like we talked about the creatinine, the creatinine may have gone up a smidge without alerting your system, may have gone by 0.3. The white count may have even doubled or tripled but may not have reached the high because these patients, in addition to having low creatinine at baseline, have low WBC count as well because hypersplenism, so the WBC count may have tripled without realizing that that's happening. So because of all these issues, it becomes harder for us to diagnose patients with infection until it is too late because these things that would alert us for infections in patients without cirrhosis are often missing. So patients who come in with acute kidney injury, even a small increase in creatinine, patients who come in with a slight increase in white count, which may be doubling of their baseline, and patients who come in with slight amount of confusion, even though they're not feeling themselves, must really be worked up for infection because an untreated infection can lead to the cascade that we mentioned before as acute-on-chronic liver failure.

Dr. Buch:
Thank you. Why should we be careful about PPI use in cirrhosis?

Dr. Bajaj:
Now PPIs have been given a bad rap. They are incredibly useful medications but for indications and the durations that they were originally prescribed for. As you and I both know, many people who are on PPI have no idea why they are on PPI and when they were started. In fact, the AGA just came out with a deprescribing PPI guidance, which will be useful. But in patients with cirrhosis, because of their impact on the oxidative burst and because of their impact on the microbiome in the saliva that often goes to the stool and can result in infections, PPI use has been potentially associated with infections, such as spontaneous bacterial peritonitis, have also been associated with hepatic encephalopathy even after controlling for all the confounding factors. And more importantly, from a fiscal and conservation of resources standpoint, the patients should not be on any medications they did not need to be on. So even if you forget all about these other associations which are important, no patient should be on a medication that they really should not be on, so now is the time to reevaluate every patient with cirrhosis that you have who is on a PPI to see why they are on PPI, how long they should be on a PPI and if you can substitute the PPI with an H2-receptor blocker, which does not have any of these infectious implications but can work just as well for occasional heartburn for these patients.

Dr. Buch:

Let's now move on to surgery. How do you assess surgical risk for cirrhotic patients?

Dr. Bajaj:
So in patients with cirrhosis, surgery is often a big precipitant, and this is the classic precipitant for acute-on-chronic liver failure because it does not have any of the inflammatory milieu that patients who develop with infection. There are certain scores. One of them is the Mayo Clinic Score, and the other one is the VOCAL-Penn Score, the websites which are listed in the actual guideline itself, that are available to calculate the risk of mortality after surgery. Now of course, the risk of mortality does not necessarily mean these patients develop acute-on-chronic liver failure after the surgery and before their death, but what it really tells you is realistic counseling for the patients and for the surgeons because often these patients come back to us as hepatologists and as GI physicians to "clear them for surgery." So the good rule is always, unless the patient is emergent, if they are decompensated cirrhosis, the only surgery they really should be going for, which is not urgent, is a liver transplant.

Dr. Buch:
We've covered a lot of ground today, but, Dr. Bajaj, I want to give you an opportunity before we conclude to talk to the audience about anything else that we did not discuss.

Dr. Bajaj:
Thank you so much for this opportunity to highlight acute-on-chronic liver failure. It is an emerging entity, but it has the potential to ensnare a lot of patients, and it is imminently preventable. There is also a companion to this that has just been published called "Guideline to Practice," which goes through a hypothetical case where multiple opportunities have been missed from patient with diagnosis of cirrhosis to infection, to aspiration pneumonia, and how this patient could have been saved, and I would urge your readers to also look at that. That's called "Guideline to Practice Acute-on-Chronic Liver Failure;" it's online already in the *American Journal of Gastroenterology*. The other thing is this is a team sport. From the emergency room physicians to the primary care physicians to hepatologists, gastroenterologists, advanced practice providers, and intensive care unit as well as palliative care practitioners, this is a disease process that requires a multidisciplinary approach and, more importantly, awareness, so I thank you again for shining a light on this and increasing awareness for acute-on-chronic liver failure.

Dr. Buch:
Well, that brings us to the end of today's program. I want to thank my guest, Dr. Jasmohan Bajaj, for helping us better understand acute-on-chronic liver failure. Dr. Bajaj, it was a pleasure having you on the program today.

Dr. Bajaj:
Same here. Thank you so much.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening and see you next time.