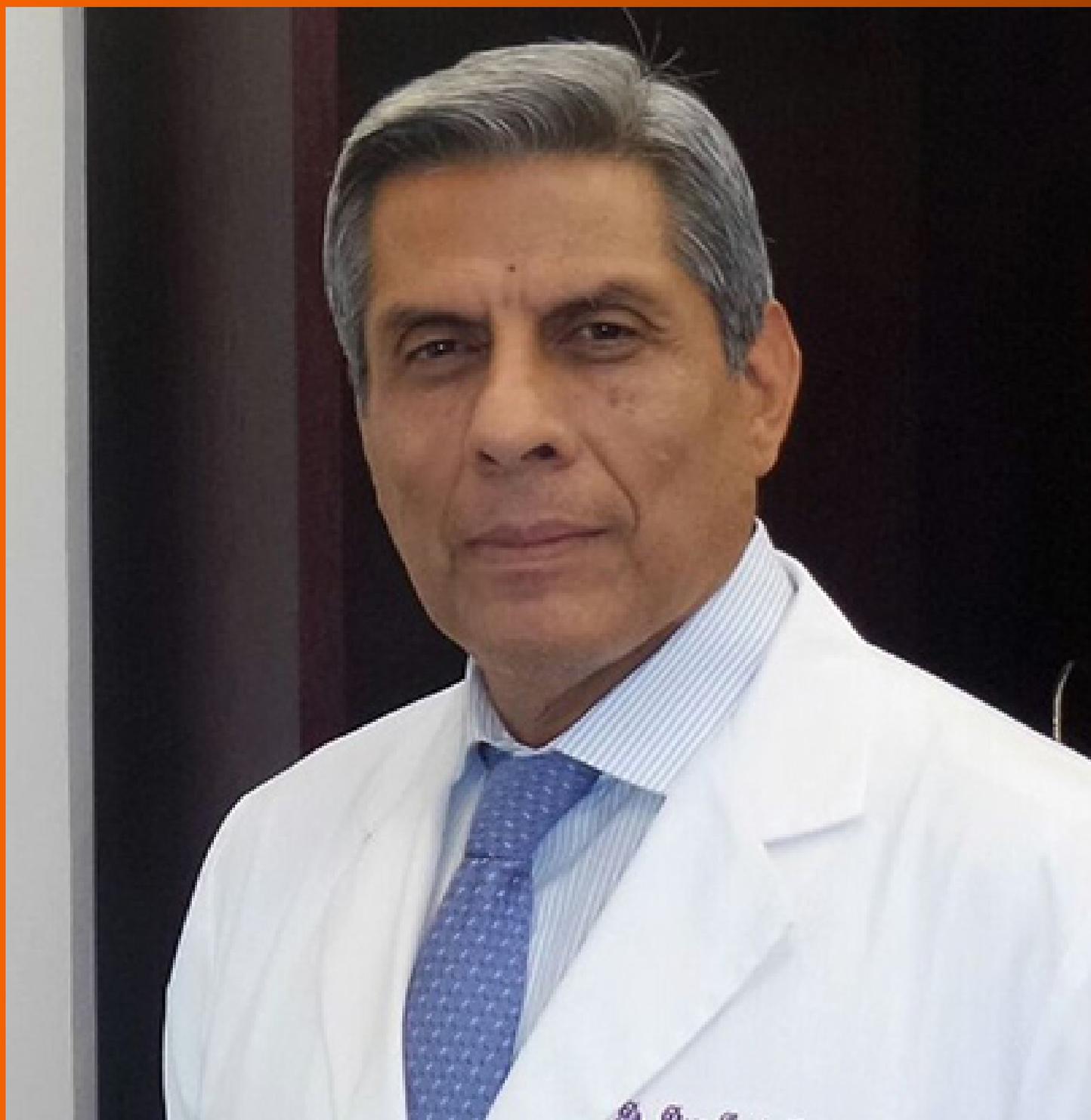


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Letter to editor 'prognostic significance of hepatic encephalopathy in patients with cirrhosis treated with Rifaximin'

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Abstract

The present letter to editor is related to Bohra A *et al* Prognostic significance of hepatic encephalopathy in patients with cirrhosis treated with current standards of care. *World J Gastroenterol* 2020; 26(18): 2221-2231. Hepatic encephalopathy (HE) is a significant and frequent major decompensating event in cirrhosis. However clinical studies examining the clinical outcome of HE are lacking despite its high prevalence.

Key Words: Hepatic encephalopathy; Cirrhosis; Rifaximin; Portal hypertension; Acute on chronic liver failure; Prognosis

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Core Tip: This letter to editor serves to add to the ongoing conversation regarding hepatic encephalopathy (HE) and its prognostic significance. The major highlight of this letter is to stress the importance of recognizing other prognostically significant variables such as sarcopenia and active Hepatitis C, which may adversely impact the severity and outcomes of HE. Furthermore it serves to actively encourage future studies in this area.

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TO THE EDITOR

We read with interest this retrospective study by Bohra *et al*^[1]. We thank the authors for sharing their real-life data in which they looked into the natural history of patients presenting to the gastroenterology inpatient service with refractory/recurrent hepatic encephalopathy (HE) and use of Rifaximin.

Rifaximin's efficacy in the treatment of acute episodes of HE, and prevention of recurrent episodes of HE has been demonstrated in several randomized control trials^[2]. Its role within these contexts has been supported by the international guidelines^[3]. The prognostic benefit of Rifaximin in the treatment of HE has also been studied. In a meta-analysis^[4] which included 5 randomized and 5 observational studies involving 2276 patients suggested that the combination therapy (rifaximin plus lactulose) reduced mortality and improved clinical efficacy. Combination therapy, as compared to treatment with lactulose alone, revealed comparable results in clinical efficacy (95%CI: 0.16–0.35, NNT 4) and mortality (95%CI: –0.33–0.12, NNT 5) when reviewing the pooled results of all the randomized studies.

In the current study by Bohra *et al*^[1], the authors concluded that the use of Rifaximin failed to have prognostic impact on the outcomes of patients with decompensated liver disease. The probability of survival at 12 mo was 44% for the entire cohort, seemingly no different to the survival figures from studies in the 'pre-rifaximin era'^[5].

However, the results should be interpreted within the context of inherent flaws of the retrospective design of the study and lack of a control arm.

As acknowledged by the authors, in the majority of cases their HE was a complication of the major prognostically significant decompensatory events including ascites, spontaneous bacterial peritonitis and gastrointestinal bleed. Therefore, simply treating HE may not have an impact on the natural progression of the disease in such an advanced stage. Not surprisingly, inpatient mortality of the patients during the same admission, prior to discharge was 22%. In a study using the Canonic database, Cordoba *et al*^[6] described a marked survival difference whether or not HE occurred in presence of acute-on-chronic liver failure (ACLF). ACLF associated with HE had poorer prognosis and occurred in context of active alcoholism, sepsis, severe liver failure as compared to patients without ACLF, where HE occurred in older cirrhotic, inactive drinkers, without evidence of systemic inflammatory response or severe liver failure and often in relation to opiates use or diuretic.

Indeed, in the current study, the two most common aetiologies include alcohol (62%) and Hepatitis C (31%) with an average total Bilirubin of 151 $\mu\text{mol/L}$ and INR 2. It is possible that a significant proportion of these patients may have active alcoholism and alcoholic hepatitis with a distinct clinical course and is associated with a high short-term mortality. Also, it would be interesting to know how many of those Hepatitis C cirrhotics had active infection as opposed to the patients who have had viral eradication, as achieving sustained virological response is associated with disease regression and prolonged survival^[7].

Finally, assessment for sarcopenia is a prognostically significant variable which also has impact on the presence and severity of HE. Its assessment would have been of immense importance in the prognostication of liver disease and mortality risks^[8].

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