Annals of Hepatology 30 (2025) 102105

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology

Letters to the editor

Comment on "outcomes and risk factors for de novo major depressive disorder after liver transplantation: Nested case-control study"

Dear Editor:

We read the study [1] with interest; it investigated the contributing factors and outcomes associated with the onset of *de novo* major depressive disorder (MDD) following liver transplantation. The objective of this nested case-control study was to evaluate the prevalence, underlying risk factors, and prospective effects of MDD on post-transplant survival and recovery. The findings indicate that MDD significantly affects liver transplant recipients, leading to reduced graft survival rates compared to controls. Female sex, alcoholic liver disease, pre-transplant encephalopathy, and inadequate hemoglobin levels were recognized as significant risk factors for the onset of MDD. The study highlights the importance of early detection and intervention for depressive symptoms in liver transplant patients, as this can significantly improve both physical and mental health outcomes. However, various elements of the findings require further examination.

First, the study [1] provides a comprehensive array of laboratory test results in Table 2, encompassing alanine aminotransferase, aspartate aminotransferase, and serum creatinine. Nonetheless, the study lacks a definitive specification regarding the precise timing of the laboratory tests—were they conducted two weeks prior to liver transplantation or merely one day before the procedure? Insufficient clarity can notably elevate the risk of measurement bias, potentially clouding the connection between laboratory values and post-transplant outcomes. Laboratory results for patients in need of liver transplantation may vary significantly due to factors including disease progression, acute liver decompensation, or other comorbid conditions. Such variations may result in considerable discrepancies in test outcomes that might not accurately reflect the patient's baseline condition. If the laboratory tests were conducted closer to the transplant date, specifically within 24 hours prior to the procedure, they would more precisely capture the patient's true clinical status and the immediate risk factors associated with liver transplantation.

Second, Table 1 of the study [1] presents data indicating that patients who developed MDD required higher red blood cell (RBC) transfusions compared to the control group, with a median of 5 L (4–10 L) versus 4 liters (1–8 L), respectively, showing a significant difference (p = 0.034). This suggests a potential connection between the need for RBC transfusions and the development of MDD in patients who have received liver transplants. However, the subsequent analysis does not explore this relationship through regression analysis or other statistical methods. Given the potential clinical importance of this association, it is recommended that this study investigate whether RBC transfusions independently contribute to the development of *de novo* MDD, while taking into consideration other confounding variables. This approach could determine whether RBC transfusions are merely a marker of disease severity or a direct risk factor for MDD in this patient population.

Third, this study [1] found that pre-transplant encephalopathy was an important risk factor for the development of de novo MDD after liver transplantation. It is important to highlight that hepatic encephalopathy (HE) and major depressive disorder (MDD) exhibit certain similarities in their clinical manifestations [2,3], potentially resulting in diagnostic confusion. HE is characterized by difficulties in attention, challenges with executive functions, and delayed responses, whereas MDD may also manifest as psychomotor retardation and inattention, especially in older adults or those experiencing severe depression. This study diagnosed MDD exclusively using DSM-IV or DSM-V criteria, which may misclassify minimal hepatic encephalopathy (MHE) symptoms as de novo MDD. It is advisable to integrate neuropsychological assessments (like PHES and BDI) to distinguish HE from MDD [4,5]. Dynamic monitoring of HE markers, including blood ammonia levels, brain MRI, or EEG, should be performed when necessary to eliminate confounding factors.

Declaration of competing interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] Yoo YJ, Lee J, Kim DG, Kang M, Koh HH, Min EK, et al. Outcomes and risk factors for de novo major depressive disorder after liver transplantation: nested case-control study. Ann Hepatol 2025;30(1):101779. https://doi.org/10.1016/j.aohep.2025.101779.

[2] Telles-Correia D, João Freire M, Mega I, Barreiras D, Cortez Pinto H. Anxiety and depression symptoms in hepatic encephalopathy: are they psychiatric or organic? Transpl Proc 2015;47(4):1005–7. https://doi.org/10.1016/j.transproceed.2015.03.011.

https://doi.org/10.1016/j.aohep.2025.102105

[3] Cooper KM, Colletta A, Osorio B, Herringshaw E, Talat A, Devuni D. History of depression is associated with higher prevalence of hepatic encephalopathy in patients with advanced liver disease. Am J Med 2024;137(9):872–9.e2. https://doi.org/10.1016/j.amjmed.2024.04.036.
[4] Malaguarnera M, Bella R, Vacante M, Giordano M, Malaguarnera G, Gargante MP, et al. Acetyl-L-carnitine reduces depression and improves quality of life in patients with minimal hepatic encephalopathy. Scand J Gastroenterol 2011;46(6):750–9. https://doi.org/10.3109/00365521.2011.565067.
[5] Warmenhoven F, van Rijswijk E, Engels Y, Kan C, Prins J, van Weel C, et al. The Beck depression inventory (BDI-II) and a single screening question as screening tools for depressive disorder in Dutch advanced cancer patients. Support Care Cancer 2012;20(2):319–24. https://doi.org/10.1007/s00520-010-1082-8.

Quanhe Zhou
Tieli Kang*
Department of Hepatobiliary Surgery, Inner Mongolia Xing'an Meng People's Hospital, Xing 'an League, Inner Mongolia Autonomous Region, 137400, China

*Corresponding author.
E-mail address: kangtieli126@163.com (T. Kang).