Journal of Nephrology

Commentary on "Challenges in the Treatment of Hepatorenal Syndrome-Acute Kidney Injury: A US Chart Review of Treatment Patterns and Survival Outcomes"

Arun J. Sanyal[1], K. Rajender Reddy[2], Kimberly A. Brown[3], Charles S. Landis[4], Giuseppe Cullaro[5], Xingyue Huang[6], Sneha S. Kelkar[7*], Rutika Raina[7], Shelby Corman[7], Nehemiah Kebede[7], Patrick Edmundson[7], Khurram Jamil[6], Andrew S. Allegretti[8]

[1]Division of Gastroenterology, Hepatology and Nutrition, Virginia Commonwealth University School of Medicine, Virginia, USA;
[2]Division of Gastroenterology and Hepatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA;
[3]Division of Gastroenterology and Hepatology, Henry Ford Health System, Detroit, USA;
[4]Division of Gastroenterology and Hepatology, University of Washington Medical Center, Seattle, USA;
[5]Division of Gastroenterology and Hepatology, University of California San Francisco, San Francisco, USA;
[6]Evidence Generation & Data Sciences, R&D, Mallinckrodt Pharmaceuticals, Hampton, USA;
[7]Real World Evidence, OPEN Health, Bethesda, USA;
[8]Division of Nephrology, Department of Medicine, Massachusetts General Hospital, Boston, USA

Correspondence to: Sneha S. Kelkar, Real World Evidence, OPEN Health, Bethesda, USA; Email: snehakelkar@openhealthgroup.com

Received date: Oct 11, 2025; **Reviewed date:** Oct 24, 2025; **Accepted date:** Oct 27, 2025; **Revised date:** Oct 31, 2025; **Published date:** Nov 07, 2025

Citation: Sanyal AJ, Reddy R, Brown KA, Landis CS, Cullaro G, Huang X, et al. (2025) Commentary on "Challenges in the Treatment of Hepatorenal Syndrome-Acute Kidney Injury: A US Chart Review of Treatment Patterns and Survival Outcomes". J Nephrol.1: 009.

DESCRIPTION

Hepatorenal syndrome with acute kidney injury (HRS-AKI), is a unique subset of AKI representing about 11-20% of HRS-AKI episodes in patients with cirrhosis [1,2]. Before the availability of terlipressin in the US in 2022, HRS-AKI therapeutic options had been limited to off-label use of varied vasopressors primarily midodrine with octreotide combination with albumin [3]. Recent studies have shown low mortality (17.6%) and substantial HRS reversal (47.6%) in patients using terlipressin, however <21% patient receive terlipressin as first-line treatment [4,5]. There is sparse evidence in literature assessing real-world treatment patterns and their impact on HRS-related outcomes. Our study aims to fill this gap prior to 2022 and establish a baseline against which future studies of terlipressin can be evaluated in the United States.

We conducted a retrospective, multicenter medical chart review study across 10 medical centers during a 4-year period from January 1, 2016-June 30, 2019 (data were collected until 2021) in the US. The objective was to describe the experience of HRS-AKI treatment, with a focus on patient characteristics, treatment patterns, clinical outcomes and healthcare resource use. In this study, we found that prior to the availability of terlipressin, hospitalized HRS-AKI patients experienced poor complete response with off-label treatments (14.6%) and high in-hospital mortality (33.8%). Median (95% CI) overall and transplant-free survival from vasopressor initiation was 48 (32-81) and 28 (19-36) days.

CONCLUSION

Our study uncovered a high disease burden and suboptimal outcomes in HRS patients before terlipressin approval. Study limitations include transcription errors inherent to using medical chart data and focus on practices of physicians from large academic hospitals where more severe patients are likely admitted. HRS-AKI is acute, difficult to diagnose, and practice patterns vary according to local standards of care. Patients referred to such tertiary centers often have a lack of access to early and approved treatments. With the evolving landscape, it is critical to understand the implication of using non-approved regimens and the barriers to access the current standard of care.

AUTHOR CONTRIBUTION

XH, KJ, ASA conceived the project and participated in reviewing study documents, results, and manuscript. SSK, RR, SC, NK, PE participated in study conduct, preparing study documents, data analysis, reviewing results, preparing manuscript. AJS, RR, KAB, CSL, GC, ASA participated in study data collection, reviewing results and manuscript.

CONFLICT OF INTEREST

Xingyue Huang is an employee of Mallinckrodt Pharmaceuticals. Khurram Jamil was an employee of Mallinckrodt Pharmaceuticals at the time this research was conducted. Sneha S. Kelkar and Rutika Raina are employees of OPEN Health, which received consulting fees related to this study. Shelby Corman, Nehemiah Kebede, and Patrick Edmundson were employees of OPEN Health at the time this research was conducted. Arun J. Sanyal, Kimberly Brown, and Charles S. Landis received research funding from Gilead, Pfizer, Lilly, and Mallinckrodt. K. Rajender Reddy is an advisor to Spark Therapeutics, Mallinckrodt, Novo Nordisk, and DSMB-Novartis; and received research support (paid to the University of Pennsylvania) from Mallinckrodt, Sequana, Grifols, Exact Sciences, BMS, Intercept, BioVie, HCC-TARGET, and NASH-TARGET. Giuseppe Cullaro and Andrew Allegretti served on advisory boards for Mallinckrodt Pharmaceuticals. Andrew Allegretti received consulting fees from Ocelot Bio, Sequana Medical, Motric Bio, and Bioporto.

REFRENCES

1. Arnold J, Avila E, Idalsoaga F, Diaz LA, Valverde MA, Ayares G, et al. Advances in the diagnosis and management of hepatorenal syndrome: Insights into HRS-AKI and liver transplantation. eGastroenterology. 2023;1(2).
2. Wong RJ, Balasubramanian J, Panaccio M, Huang X. Acute kidney injury and hepatorenal syndrome among hospitalized patients with chronic liver disease. JAMA Netw Open. 2025;8(5):e2511816.
3. Biggins SW, Angeli P, Garcia-Tsao G, Gines P, Ling SC, Nadim MK, et al. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American association for the Study of Liver Diseases. Hepatology. 2021;74(2):1014-1048.
4. Patidar KR, Belcher JM, Regner KR, St Hillien SA, Simonetto DA, Asrani SK, et al. Incidence and outcomes of acute kidney injury including hepatorenal syndrome in hospitalized patients with cirrhosis in the US. J Hepatol. 2023;79(6):1408-1417.
5. Wong R, Allegretti AS, Huang X, Panaccio MP, Cardoza S, Niewoehner J, et al. S1957 Trends in the early adoption of terlipressin among hospitalized adults with hepatorenal syndrome in the US: A Real-world analysis. Official journal of the American College of Gastroenterology| ACG. 2024;119(10S):S1400-S1401.