Increasing Burden of Hepatorenal Syndrome and Acute Kidney Injury among Hospitalized Patients with Chronic Liver Disease is Associated with High In-Hospital Mortality and Increased Healthcare Resource Utilization

RJ Wong[1], J Balasubramanian[2], K Jamil[2], X Huang[2]

1. Stanford University School of Medicine, Palo Alto, CA; 2. Mallinckrodt Pharmaceuticals, Hampton NJ, USA

BACKGROUND

- Hepatorenal syndrome (HRS) is a severe form of acute kidney injury (AKI) that develops in patients with decompensated liver disease and is associated with high morbidity and mortality.[1]
- Understanding epidemiologic trends in HRS and AKI among chronic liver disease (CLD) patients will provide valuable data to guide healthcare resource planning.

OBJECTIVE

- We aimed to evaluate trends in hospitalized patients with CLD and HRS or AKI in the US and the impact on in-hospital mortality and healthcare resource utilization (HCRU).

MATERIAL AND METHODS

- A retrospective, longitudinal analysis of the Premier Healthcare Database (PHD) was conducted to first identify hospitalized patients with chronic liver disease (CLD, based on ICD-10 codes, Hirode et al 2020)[2] between 2016 and 2021.
- PHD is one of the most comprehensive, HIPAA-compliant electronic healthcare databases with more than 1,041 contributing hospitals/healthcare systems in the US.
- Patient selection criteria:
  - HRS patient cohort: Adult patients hospitalized with a diagnosis of CLD and hepatorenal syndrome (HRS, ICD-10 code K76.7) between 2016 and 2021.
  - AKI patient cohort: Adult patients hospitalized with a diagnosis of CLD and acute kidney injury (AKI, ICD-10 codes N17.x) between 2016 and ▶ 2021
- Outcomes of interest
  - Trends in in-hospital mortality and health care resource use (HCRU, hospital length of stay (LOS), total hospitalization charges) were evaluated for CLD patients with HRS or AKI.
  - Annual incidence rates for patients with HRS or AKI in the US were calculated using estimates based on AHA (American Hospital Association) inpatient projection weight in the PHD database.[3]
- All analyses were conducted using Databricks platform.

RESULTS

Patient population

- A total of 3,580,434 hospitalizations with CLD were identified, representing approximately 6.7% of all hospitalizations during the study period (2016-2021).
- Among the CLD patients, 1,005,287 (28.1%) had a diagnosis of AKI, with mean age of 62.2 years, 59.7% were males, and 54.1% under Medicare (Table 1).
- Among the CLD patients, 72,675 (2.0%) had a diagnosis of HRS, with mean age of 59.0, 61.0% of males, and 43.0% under Medicare (Table 1).

Table 1. Patient demographics, clinical characteristics and insurance

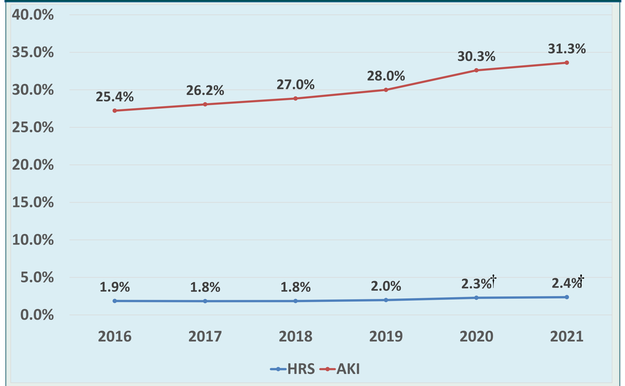
		All CLD (N=3,580,434)	AKI (n=1,005,287)	HRS (n=72,675)
Age, years, mean [median] [std]		57.4 [59.0] [15.7]	62.2 [63.0] [14.6]	59.0 [60.0] [13.1]
LOS, days, mean [median] [std]		6.7 [4.0] [11.5]	9.6 [6.0] [12.6]	10.3 [7.0] [11.4]
Gender	Female	1,589,544 [44.4%]	405,471 [40.3%]	28,319 [39.0%]
	Male	1,990,450 [55.6%]	599,673 [59.7%]	44,340 [61.0%]
	Unknown	440 [0.0%]	143 [0.0%]	16 [0.0%]
Comorbid-conditions	Ascites	614,305 [17.2%]	245,946 [24.5%]	55,075 [75.8%]
	Sepsis	630,612 [17.6%]	339,549 [33.8%]	22,455 [30.9%]
	Alcohol	1,075,267 [30.0%]	277,766 [27.6%]	41,881 [57.6%]
	Diabetes	1,255,424 [35.1%]	439,887 [43.8%]	25,658 [35.3%]
Insurance	Commercial	706,922 [19.7%]	174,210 [17.3%]	16,462 [22.7%]
	Medicaid	930,053 [26.0%]	207,067 [20.6%]	18,820 [25.9%]
	Medicare	1,592,951 [44.5%]	543,510 [54.1%]	31,216 [43.0%]
	Other*	305,169 [8.5%]	68885 [6.9%]	4985 [6.9%]
	Unknown	453,39 [1.3%]	11,615 [1.2]	11,92 [1.6%]

* Including charity, indigent, self pay, workers compensation, and other government payors.

Table 2. Hospital length of stay, in-patient mortality, and total charges

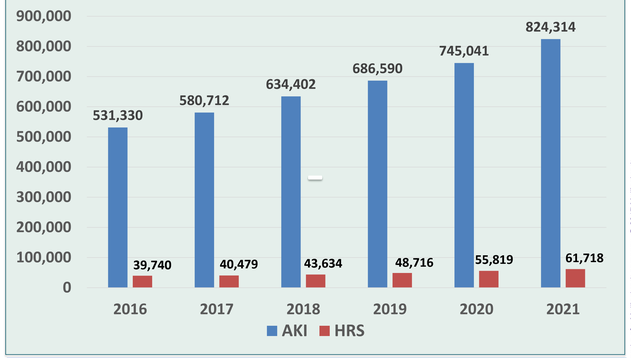
		2016	2017	2018	2019	2020	2021
AKI	N	134,291	156,666	166,400	178,618	179,355	189,957
	LOS	9.3 [6.0]	9.3 [6.0]	9.3 [6.0]	9.3 [6.0]	9.7 [6.0]	10.3 [6.0]
	Mean total charges [median]	$106,194 [$54,538]	$114,993 [$58,751]	$122,257 [$61,372]	$131,239 [$64,916]	$141,955 [$69,822]	$155,314 [$75,501]
	Inpatient Mortality, N [%]	23,307 [17.4%]	27,602 [17.6%]	28,796 [17.3%]	29,893 [16.7%]	34,368 [19.2%]	39,546 [20.8%]
	Liver Transplant N [%]	447 [0.3%]	581 [0.4%]	678 [0.4%]	890 [0.5%]	843 [0.5%]	829 [0.4%]
	Kidney Transplant N [%]	97 [0.1%]	99 [0.1%]	98 [0.1%]	128 [0.1%]	122 [0.1%]	135 [0.1%]
HRS	N	9,838	10,955	11,388	12,610	13,513	14,371
	LOS	10.2 [7.0]	10.2 [7.0]	10.0 [7.0]	10.3 [7.0]	10.4 [7.0]	10.6 [7.0]
	Mean total charges [median]	$111,665 [$60,802]	$123,493 [$66,826]	$131,775 [$69,044]	$142,023 [$75,711]	$152,298 [$79,024]	$154,316 [$82,604]
	Inpatient Mortality N [%]	2,703 [27.5%]	3,007 [27.4%]	3,013 [26.5%]	3,176 [25.2%]	3,414 [25.3%]	3,773 [26.3%]
	Liver Transplant N [%]	164 [1.7%]	213 [1.9%]	231 [2.0%]	303 [2.4%]	333 [2.5%]	327 [2.3%]
	Kidney Transplant N [%]	45 [0.5%]	49 [0.4%]	40 [0.4%]	62 [0.5%]	55 [0.4%]	59 [0.4%]

Figure 1. Percentage of HRS and AKI among Hospitalized CLD Patients**



** All AKI trends are statistically significant with p <0.001.
† Statistically significant (p<0.005)

Figure 2. Estimated Annual Inpatient Counts of HRS and AKI in the US



LIMITATIONS AND CONCLUSIONS

Limitations

- The analysis is based on the PHD database and is affected by misclassification bias associated with the hospital patient level encounter data.
- Patients with CLD, HRS and AKI were identified based on diagnosis codes (ICD-10) on the hospital claim.
- The estimated annual incidences of HRS and AKI were based on the AHA inpatient projection weight designed to project national inpatient counts (based on the AHA Annual Survey Database™)[3].

Conclusions

- The burden of CLD hospitalizations in the US continues to rise.
- The increasing burden of hospitalized CLD patients with HRS or AKI is particularly concerning, given that these patients have significantly greater co-morbidities, high HCRU, and high mortality, highlighting the clinical and economic burden of HRS and AKI among CLD patients in the US.

References

1. Biggins 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
2. Hirode et al Trends in the Burden of Chronic Liver Disease Among Hospitalized US Adults. JAMA Network Open. 2020;3(4):e201997. doi:10.1001/jamanetworkopen.
3. Premier Healthcare Database White Paper: Data that informs and performs, July 29, 2018. Premier Applied Sciences®, Premier Inc. https://learn.premierinc.com/white-papers/premier-healthcaredatabase-whitepaper.

American College of Gastroenterology Annual Meeting, Charlotte, NC, Oct 23-26, 2022

Acknowledgement: This study was funded by Mallinckrodt Pharmaceuticals (Hampton, NJ, USA). Contact: Xingyue.Huang@mnk.com
Disclosures: RJW serves as a clinical expert on this project and has no financial relationship with Mallinckrodt Pharmaceuticals. JB, KJ and XH are employees of Mallinckrodt Pharmaceuticals.