JIM Research Letter

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Increased mortality of patients with alcohol-related liver diseases during the COVID-19 pandemic in the United States

Dear Editor,

Stress related to the coronavirus 2019 (COVID-19) pandemic could lead to excessive alcohol use, which can be further aggravated by isolation-related boredom, shifted medical resources, and limited access to mental health care [1, 2]. Prior single-center studies showing increased prevalence of alcohol-related liver disease (ALD) were limited by selection bias [3, 4]. Except for increasing prevalence, data on ALD-related mortality before and during the pandemic were limited. Here, we determined and compared the 60- and 90-day mortality rates of U.S. patients with ALD before and during the pandemic using a national database.

Data were obtained from Optum™ Clinformatics™ DataMart, a resource of the Population Health Science Center at Stanford University. The study was approved by the Institutional Review Board at Stanford University. Enrollees with alcohol use disorder (AUD) diagnoses receiving care in hospital emergency departments and/or inpatient services during January 1, 2019 to December 31, 2020 were included and followed up until March 31, 2021. ALD and AUD were defined by the International Classification of Diseases 10th revision (ICD-10) codes. We estimated the quarterly 60- and 90-day mortality rates and prevalence of ALD. We defined the pre-COVID pandemic period as 2019 Q1 to 2020 Q1 and COVID-19 pandemic as 2020 Q2 to 2021 Q1. By comparing to the same quarter in 2019, we performed multivariable log-binomial regression adjusting for age, sex, and race/ethnicity to determine the risk of 60- and 90-day mortality in each quarter during the pandemic. We also used interrupted time series regression to determine the changes of mortality rates over time to evaluate the impact of the COVID-19 pandemic on mortality [5].

A total of 25,721 patients with ALD admitted to emergency departments or inpatient care were identified, including 16,813 patients before and 11,625 during the pandemic (Table 1). A majority of the patients were admitted to inpatient care, while 3.98% of ALD patients were admitted to emergency department only. About half of the patients were aged 65 years and above. Males constituted about two-third of the ALD patients. Non-Hispanic Whites (64.13%) represented the largest group of patients, followed by Hispanic and non-Hispanic Blacks. Non-Hispanic Asians only constituted 1.40% of the ALD patients.

During the pre-pandemic period, there was a downward trend in both 60-day and 90-day mortality rates among patients with ALD who were admitted to emergency departments or inpatient services between 2019 Q1 and 2019 Q3, then went up in 2019 Q4 and 2020 Q1 (Fig. 1). However, during the pandemic (2020 Q2 and onward), the trends of both 60- and 90-day mortality were consistently up throughout. Notably, by the end of 2020, about one in four patients with ALD from the emergency department and inpatient wards died by 90 days (2020 Q4, 90-day mortality = 24.75%) and one in five patients died by 60 days (60-day mortality = 21.19%). Data from interrupted time series regression also confirmed that while the odds of death for ALD during the pre-pandemic era declined slightly (0.995, $p < 0.01$), the odds of ALD death surged following the pandemic onset during 2020 Q2 (18.73, $p < 0.01$), with a slight decline thereafter (0.990, $p < 0.01$).

In addition, a quarterly comparison between 2020 and 2019 showed that the adjusted prevalence ratio in 60- and 90-day mortality rates of ALD significantly increased for all quarters (Fig. 2) except the first quarters, both of which fell in the pre-pandemic era (2019 Q1 vs. 2020 Q1). In fact, 60-day mortality increased 45% between 2020 Q2 compared to 2019 Q2 (adjusted ratio: 1.45, 95% confidence interval [CI] 1.29–1.63).

Table 1. *Baseline characteristics of alcohol-related liver disease (ALD) patient admitted to emergency department or inpatient during the study period, categorized by period before and during the pandemic*

	Overall N = 25,721 (%) (2019–2020)	Pre-pandemic N = 16,813 (2019 Q1–2020 Q1) N (%)	Pandemic N = 11,625 (2020 Q2–Q4) N (%)
Admission type			
Inpatient	24,697 (96.02%)	16,134 (95.96%)	11,091 (95.41%)
Emergency	1024 (3.98%)	679 (4.04%)	534 (4.59%)
Age			
21–44	2734 (10.63%)	1705 (10.14%)	1257 (10.81%)
45–64	10,382 (40.36%)	6856 (40.78%)	4757 (40.92%)
≥65	12,605 (49.01%)	8252 (49.08%)	5611 (48.27%)
Sex			
Male	17,625(68.52%)	11,529 (68.57%)	7966 (68.52%)
Female	8093 (31.46%)	5282 (31.42%)	3658 (31.47%)
Race/ethnicity			
Hispanic	3163 (12.30%)	2127 (12.65%)	1387 (11.93%)
Non-Hispanic Whites	16,458 (63.99%)	10,735 (63.85%)	7514 (64.64%)
Non-Hispanic Blacks	2668 (10.37%)	1720 (10.23%)	1222 (10.51%)
Non-Hispanic Asians	376 (1.46%)	253 (1.50%)	158 (1.36%)

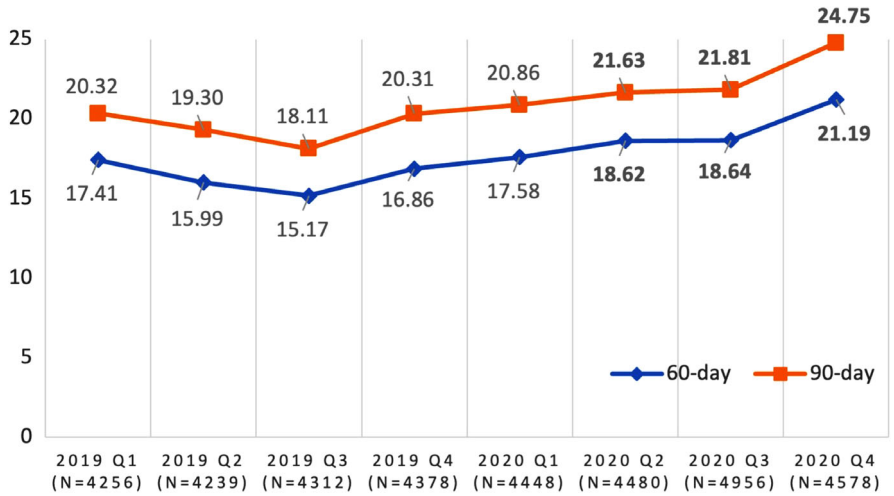

Fig. 1 *Mortality rates for alcohol-associated liver disease in adults aged 21 years or older who visited the emergency department or was admitted. Quarterly 60- and 90-day mortality rate between January 2019 and December 2020.*

Using population-based longitudinal data, we demonstrated an alarming rise in 60- and 90-day mortality rates in patients with ALD who were admitted to emergency departments or were inpatients during the pandemic. This could be due to the direct impact of COVID-19 and its indirect effect on the healthcare system, including delays in presenting to medical attention or medical management due to stay-at-home policy or inadequate medical resources. The increase in alcohol use and stress during the pandemic also add to the toll. Mounting evidence has indicated increased retail alcohol sales [6] and rising prevalence in ALD or alcohol-related emergencies during the pandemic [4].

Our study has limitations. Our data were derived from patients with private insurance, and those who lost employment and insurance coverage during the pandemic were not recorded. However, the uninsured/underinsured and those who lost insurance are likely more vulnerable to the effect

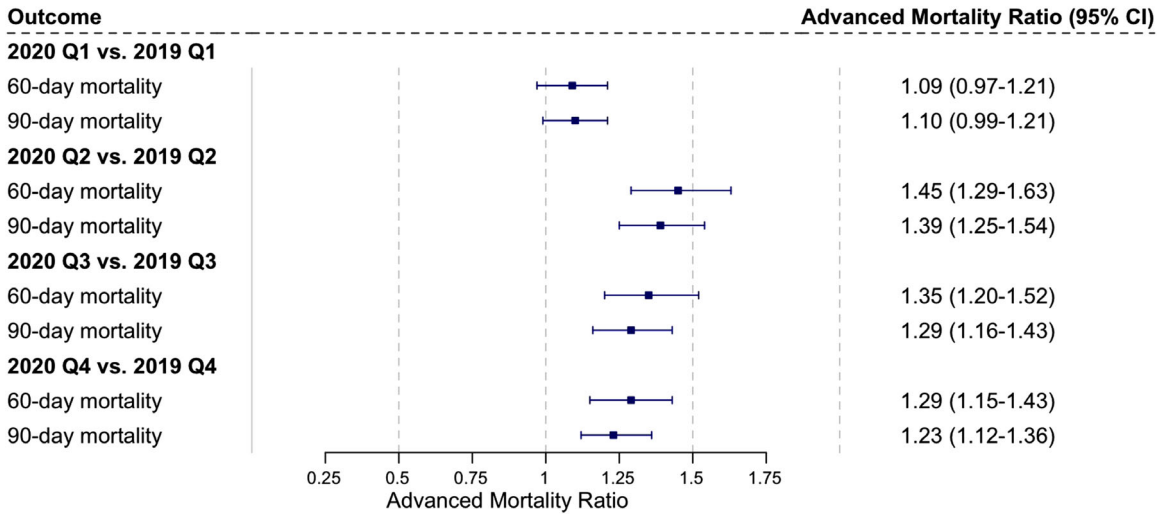

Fig. 2 *Adjusted prevalence ratio of quarterly 60- and 90-day alcohol-associated liver disease-related mortality rates in 2020 compared with corresponding quarters in 2019. Adjusting factors: age, sex, race/ethnicity. CI: confidence interval.*

of COVID-19 pandemic, but these would only bias toward lower prevalence and mortality rate.

Our findings call for more targeted interventions and resource allocation to curb the surging burden of ALD. Specifically, mental health services and alcohol treatment programs should be more available during a pandemic, and not less.

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Conflict of interest

The authors declare no conflict of interest.

Author contributions

Study conception and study supervision: MHN. Study design and methodology: YHY, BZ, and MHN. Data curation and analysis: BZ. Visualization: YHY and BZ. Drafting of the manuscript: YHY and MHN. Data interpretation and critical review of the manuscript: All authors.

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