Increased mortality in patients with alcohol-induced pancreatitis during the COVID-19 pandemic

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Abstract	Background COVID-19 pandemic affected millions of people worldwide. Alcohol consumption increased during the pandemic, leading to rising numbers of cases of alcohol-related pancreatitis. We aimed to assess the mortality of alcohol-induced pancreatitis during the COVID-19 pandemic in the United States.
	Methods We analyzed the National Vital Statistical System's (NVSS) provisional multiple causes of death data, provided by the Centers for Disease Control and Prevention, to assess the mortality of alcohol-induced pancreatitis during the pandemic. Patients with alcohol-induced pancreatitis as a cause of death were analyzed between 2018 and 2021. Patient demographics such as age, sex, ethnicity, and location were studied.
	Results During 2018-2021, there were 2547 deaths from alcohol-induced pancreatitis. The total cases and age-adjusted rates of alcohol-induced pancreatitis per 100,000 were similar in 2018 (n=515) and 2019 (n=501) (crude rate=0.1). The number increased to 747 in 2020 and 784 in 2021 (crude rate=0.2). A statistically significant increase in mortality rates was noted in all age groups except 75-84. An increase in mortality in both males and females was noted (48% increase and 64% increase, respectively, P<0.001). The number of deaths increased in both Hispanics (59%, P<0.001) and non-Hispanics (48%, P<0.001).
	Conclusions Our analysis demonstrated a substantial increase in the mortality of patients with alcohol- induced pancreatitis during the first 2 years of the COVID-19 pandemic. The increase in alcohol consumption and the burden on mental health caused massive collateral damage to society. Urgent public health interventions are needed at state and national levels to prevent further rise in cases.
	Keywords Alcohol-induced pancreatitis, acute pancreatitis, COVID-19, pandemic, mortality
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Introduction

COVID-19 pandemic triggered a public health crisis that affected medical, social and psychological wellness on a large scale [1]. The world saw an increase in depression and anxiety by 25% [2]. In previous studies, it was found that stressors lead to increased alcohol use [3]. Similarly, recent studies showed a significant increase in alcohol intake during the pandemic. Those with depressive symptoms had 64% greater odds of increased alcohol use. The reasons for increased alcohol consumption included increased stress, alcohol availability and boredom [4,5].

One of the major complications of excess alcohol consumption is alcohol-induced pancreatitis. Ethanol causes pancreatic injury by its effect on the intrapancreatic digestive enzyme action. It is known to be a primary cause of both acute and chronic pancreatitis in most developed countries, accounting for about one-third of the cases of acute www.annalsgastro.gr pancreatitis in the United States (US) [6-8]. Recent studies have revealed that, as a result of the increased alcohol intake during the pandemic, there has been a significant rise in hospital admission rates for alcohol-induced pancreatitis [9,10]. We aimed to assess the mortality of alcohol-induced pancreatitis during the COVID-19 pandemic in the US.

Materials and methods

We analyzed the National Vital Statistical System's (NVSS) provisional multiple causes of death data. These files include final mortality data for patients in the US during 2018 and 2020 and provisional mortality data for 2021. It provided quarterly estimates regarding near real-time US mortality data during the COVID-19 pandemic. We accessed data on August 7, 2022, using Centers for Disease Control and Prevention's Wideranging 5 Online Data for Epidemiologic Research (CDC-WONDER), a free web-based platform. These data were last updated on February 6, 2022, by NVSS.

The National Center for Health Statistics collects mortality data based on death certificates that are completed according to 8 instructions [11]. Death certificates include a single underlying cause of death, up to 20 additional multiple causes of death, and demographic data. Causes of death are coded according to the International Classification of Diseases, Tenth Revision (ICD-10). We identified deaths involving alcoholinduced pancreatitis (ICD-10 code K85.2).

All diagnoses listed on a death certificate must be part of the causal pathway of events and conditions leading to death, or be a significant condition that contributed to death. We defined death from a particular condition as the condition's inclusion on the death certificate, regardless of whether the condition was a contributing or underlying cause. We calculated age-adjusted death rates using the standard US population in the year 2000. For alcohol-induced pancreatitis deaths occurring from January 2018 to December 2021, we examined the numbers, percentages, and age-adjusted rates by year.

To visualize trends in alcohol-induced pancreatitis, we examined the monthly number of deaths. We examined numbers, percentages, and age-adjusted rates of death by sex, race/ethnicity, and US regions. We also examined crude death rates across age groups and urban-rural 2013 classifications of residence. Crude death rates were shown for urban-rural classifications, because age-stratified death rates by urban-rural classification were unavailable on CDC-WONDER. We compared categorical variables using the chi-square test to assess differences between the year of presentation. We categorized race/ethnicity as Hispanic or Latino or non-Hispanic and studied their trends.

Results

Demographics

During 2018-2021, there were 2547 deaths from alcoholinduced pancreatitis (Table 1). The number and age-adjusted rates of alcohol-induced pancreatitis per 100,000 were similar in 2018 (n-515) and 2019 (n-501) (crude rate for both years = 0.1).The number increased to 747 in 2020 and 784 in 2021 (crude rate for both years = 0.2). A statistically significant increase in mortality rates was noted in all age groups except the 75-84 age group (P<0.001). An increase in mortality in both males and females was noted during the COVID-19 pandemic (P<0.001). A 48% increase in deaths was noted in males between 2018 and 2021, while deaths in females increased by 64%. The number of deaths, stratified by sex, is presented in Fig. 1. The majority of deaths were noted in the non-Hispanic population. The number of deaths in the Hispanic population increased from 44 in 2018 to 70 in 2021 (59% increase, P<0.001), while the number of deaths in non-Hispanics increased from 471 in 2018 to 711 in 2021 (reflecting a 48% increase, P<0.001). A complete list of patient demographics is presented in Table 1.

Monthly distribution of deaths from alcohol-induced pancreatitis

The median monthly death in 2018 and 2019 was 44 and 39.5 respectively, while the number increased to 65 in both 2020 and 2021. A sharp increase in deaths was noted in March 2020 (n=52) and the numbers continued to rise until September (n=70). The monthly distribution of cases is presented in Fig. 2 and the Supplementary Table 1.

Mortality by region

The number of deaths increased in all US regions. Most deaths were seen in the South (n=261), followed by the West (n=256) in 2021. Although the South had the highest number of cases, the increase in cases from 2018 was higher in the West, Northeast and Midwest (58% increase in all 3 regions compared to 41% in the South). A statistically significant difference between various years was noted in all regions. These results are depicted in Fig. 3.

Discussion

Our analysis found >1500 deaths in the US from alcoholinduced pancreatitis during the COVID-19 pandemic from 2020-2021. It also revealed that the age-adjusted death

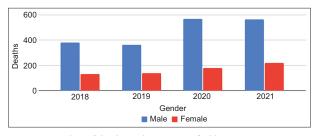


Figure 1 Number of deaths each year, stratified by sex

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	Number of deaths	Age-adjusted/ Crude rate	Number of deaths	Age-adjusted/ Crude rate	Number of deaths	Age-adjusted/ Crude rate	Number of deaths	Age-adjusted/ Crude rate	
Total number	515	0.1	501	0.1	747	0.2	784	0.2	<0.001
Age group (years)									
15-24	Unreliable data	+	12	+	16	<₽-	10	<₽-	0.002
25-34	47	0.1	63	0.1	103	0.2	94	0.2	<0.001
35-44	95	0.2	85	0.2	151	0.4	177	0.4	<0.001
45-54	136	0.3	109	0.3	148	0.4	185	0.5	<0.001
55-64	147	0.3	141	0.3	201	0.5	184	0.4	<0.001
65-74	56	0.2	70	0.2	93	0.3	97	0.3	0.011
75-84	26	0.2	18	ŧ	28	0.2	35	0.2	0.17
Sex									
Male	382	0.2	362	0.2	567	0.3	565	0.3	<0.001
Female	133	0.1	139	0.1	180	0.1	219	0.1	<0.001
Race/Ethnicity									
Hispanic/Latino	44	0.1	44	0.1	70	0.1	70	0.1	0.012
Not Hispanic/Latino	471	0.2	456	0.2	676	0.2	711	0.2	<0.001
Urban-rural 2013 classification of residence	ation of residence								
Metropolitan									
Large central metro	390	0.1^{*}	388	0.1^{*}	565	0.2*	608	0.2*	< 0.001
Large fringe metro	72	0.1^{*}	76	0.1^{*}	120	0.1^{*}	137	0.2^{*}	<0.001
Medium metro	97	0.1^{*}	06	0.1^{*}	146	0.2*	160	0.2*	<0.001
Small metro	44	0.1*	55	0.2*	62	0.2*	68	0.2*	0.15
Non-metropolitan									
Micropolitan+	43	0.2^{*}	45	0.2*	55	0.2*	58	0.2^{*}	0.35
Non-core+	23	0.1^{*}	28	0.1^{*}	28	0.1^{*}	41	0.2^{*}	0.11

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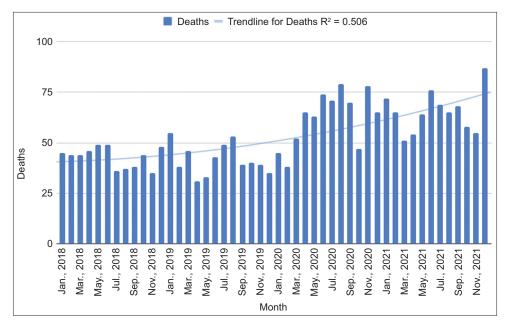


Figure 2 Monthly distribution of deaths. Lockdown began in March 2020, coinciding with the increased mortality rates observed starting March 2020

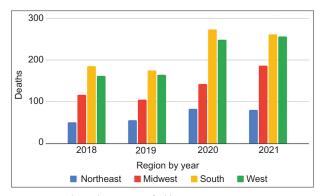


Figure 3 Deaths each year, stratified by region

rates due to alcohol-induced pancreatitis doubled from 0.1 (2018-19) to 0.2 (2020-21), and the death count rose 1.5 times from 515 (2018) to 784 (2021). The number of deaths showed a significant rise beginning in March 2020, coinciding with the beginning of lockdown. This was similar to the results of the study conducted by Sohal *et al*, which revealed a 69% increase in cases of alcohol-related hepatitis following the implementation of lockdown measures [12]. Our finding was also in agreement with the rise in admission rates for alcohol-related hepatitis and pancreatitis observed by Shaheen *et al* and Itoshima *et al* with the initiation of the lockdown [9,13]. The increase in alcohol-related disease can be attributed to the increase in alcohol sales by 55% at the beginning of stay-athome orders compared to previous years [14].

The rise in the number of deaths was 1.64 times higher among women compared to men (1.48 times). Multiple studies have elucidated the impact of the pandemic on women across the US, because of disproportionate job losses, the impact of prolonged school closures, reduced social interactions, and higher overall stress levels [15,16]. A survey published in

the Journal of the American Medical Association revealed a 41% increase in heavy alcohol consumption among women in the first several months of the COVID-19 pandemic [17]. Itoshima et al reported that the increase in admission rates for alcohol-related pancreatitis during the COVID-19 pandemic was higher in females than in males [9]. Jacob et al found that 63% of women reported increased alcohol consumption, whereas only 36% of men reported increased alcohol intake, which explains the increase in admissions and mortality in women [18]. Furthermore, Thibaut et al found that women were at higher risk for psychiatric symptoms compared to men during the pandemic, which could also explain the increased alcohol consumption [19]. The rise of alcohol use in women is of significant concern, and further studies are needed to investigate outcomes based on sex differences during the COVID-19 pandemic.

The pandemic significantly impacted the well-being of many around the world. Common risk factors associated with mental distress during the COVID-19 pandemic include female sex, younger age group (\leq 40 years), presence of chronic/psychiatric illnesses, unemployment, student status, and frequent exposure to social media/news concerning COVID-19 [20]. The biggest contributors were concerns related to risk of infection transmission, financial concerns stemming from unemployment, unsteady income and impact on social life [21,22]. Rehm *et al* predicted that there would be an increase in alcohol consumption in certain populations due to the distress experienced as a result of the pandemic [23]. The growing psychological crisis has led to significantly increased alcohol consumption, which likely to have contributed to the above findings [4,5,24,25].

Our study had several limitations. First, it could not reveal a relationship between individual alcohol consumption and deaths due to alcohol-induced pancreatitis. Therefore, further research is needed to confirm this association. Our use of broad single-race categories limited the level of detail with which we could assess racial/ethnic disparities, particularly among multiracial people. Furthermore, we were not able to assess underlying medical conditions among patients predisposed to alcohol-induced pancreatitis, since the CDC-WONDER platform does not allow the tabulation of more than 2 sets of conditions in combination. Lastly, data based on ICD-10 codes for alcohol-induced pancreatitis are subject to imprecision in reporting and underreporting. In focusing only on deaths, our analysis did not address the considerable long-term morbidity faced by certain survivors of alcohol-induced pancreatitis.

Our analysis demonstrated the substantial burden of alcohol-induced pancreatitis in the US during the first 2 years of the COVID-19 pandemic. Alcohol-induced pancreatitis was associated with significant morbidity, mortality and societal cost. The increase in alcohol consumption and the burden on mental health during the COVID-19 pandemic caused significant collateral damage to society. Urgent public health interventions are needed at state and national levels to prevent a further rise in cases from becoming the new normal. Focus on mental health, availability of therapy and support groups are crucial to overcoming these findings.

Summary Box

What is already known:

- Acute pancreatitis is a very common disease and is costly to the United States (US) healthcare system
- Acute pancreatitis is associated with significant morbidity and mortality
- There was an increase in alcohol consumption and sales during the COVID-19 pandemic

What the new findings are:

- Increased mortality of alcohol-induced pancreatitis during the COVID-19 pandemic in all age groups, except 75-84
- Increased mortality in both males and females, with a higher rate in females
- Increased mortality in both Hispanic and non-Hispanics, with a higher rate in Hispanics
- Increased mortality in all US regions, with highest rates in South and West

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Supplementary material

Months No. of deaths Jan 2018 45 Feb 2018 44 Mar 2018 44 Apr 2018 46 May, 2018 49 Jun 2018 49 Jul 2018 36 Aug 2018 37 Sep 2018 38 Oct 2018 44 Nov 2018 35 Dec 2018 48 Jan 2019 55 Feb 2019 38 Mar 2019 46 Apr 2019 31 May, 2019 33 Jun 2019 49 Aug 2019 53 Sep 2019 39 Oct 2019 40 Nov 2019 39 Dec 2019 35 Jan 2020 45 Feb 2020 38 Mar 2020 52 Apr 2020 65 May, 2020 63 Jun 2020 74 Jul 2020 74
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Supplementary Table 1 Monthly distribution of deaths