

Research article

The Incidence and Severity of Inpatient Hospital Admissions for Concomitant Covid-19 and Acute Pancreatitis and the Associated Racial Disparities

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Abstract

COVID-19 has been associated with gastrointestinal intestinal symptoms, including acute pancreatitis. Presented is a population-based analysis evaluating the association between COVID-19 and acute pancreatitis. Methods: A retrospective analysis of the 2020 Healthcare Cost and Utilization Project National Inpatient Sample was performed to compare hospital outcomes in those diagnosed with acute pancreatitis compared to those with concomitant acute pancreatitis and COVID-19. A subgroup analysis of race was performed to identify racial disparities between the two cohorts. Results: A total of 423,550 weighted inpatient discharges of acute pancreatitis were included, 2.4% had a concomitant diagnosis of COVID-19. Those with concomitant COVID-19 had increased complication rates, mean length of stay, and mortality. COVID-19 was an independent risk factor of death (aOR = 4.24, $p < 0.001$). Race varied significantly between cohorts, particularly among White (63.8% vs 39.0%) and Hispanic (13.6% vs 31.1%) groups. The adjusted odds of concomitant acute pancreatitis and COVID-19 in the Hispanic population greater compared to other races (aOR = 2.92, $p < 0.001$). Mean length of stay and death rate in the COVID-19 cohort increased most in the Asian (3.13% vs 22.40%) and Native American (2.44% vs 22.60%) populations. Discussion: Those hospitalized with acute pancreatitis should be screened for COVID-19 on admission to prevent delays in care. If diagnosed with concomitant acute pancreatitis and COVID-19, both conditions should be aggressively treated to reduce morbidity and mortality. Increased efforts at primary prevention of COVID-19 should be directed toward the Hispanic, Native American, and Asian populations in the United States.

Keywords: Acute pancreatitis, COVID-19, Epidemiology, Health disparities, Outcomes research, Racial/ethnic disparities

Introduction

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has impacted over 750 million people resulting in over 6.8 million deaths worldwide [1]. COVID-19 is generally thought of as a respiratory illness, however multiple case reports have been published reporting associated gastrointestinal conditions with the diagnosis of COVID-19, including acute pancreatitis. While gallstones and alcohol use are the most common etiologies of acute pancreatitis, viruses are also known causes, including mumps, coxsackie, hepatitis B, and cytomegalovirus [2-3]. It is

proposed that SARS-CoV-2 enters cells via the angiotensin-converting enzyme 2 (ACE2) receptor [4-6]. ACE2 is expressed in multiple organs including alveolar cells of the lung, thus resulting in COVID-19 associated respiratory failure. ACE2 is also expressed at high levels in pancreatic islet B-cells and exocrine tissue capillaries [2-4]. It is hypothesized that SARS-CoV-2 could directly cause a local immune response in the pancreas through interaction with pancreatic ACE2 receptors. Alternatively, the pancreatitis may occur secondary to indirect effects of systemic inflammation caused by SARS-CoV-2 [2].

While efforts are being made to explore these cellular mech-

anisms, it is equally vital to understand the interaction of acute pancreatitis and COVID-19 on an epidemiological level. While several case reports have been published documenting this interaction, there are no population-based analyses evaluating the association between COVID-19 and acute pancreatitis. In this analysis, the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) was used to characterize and compare the incidence and severity of hospitalizations for acute pancreatitis in those with and without a concomitant diagnosis of COVID-19. Demographic data, severity of outcomes, and racial disparities were characterized.

Methods

Data source

A retrospective analysis of the 2020 dataset from the HCUP NIS was performed. The NIS is a publicly available all-payer hospital inpatient database that contains 20% of all inpatient discharges in the United States. Weighted estimates are provided by HCUP to create national estimates of healthcare utilization and outcomes. It is important to note that the NIS represents discharges and not patient-level data. Finally, the NIS is a limited data set that does not require institutional review board approval, per the Health Insurance Portability and Accountability Act.

Study Population and Design

Included were all adult, ages 18 years and older, discharges with a diagnosis of acute pancreatitis, as defined by International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes K85.0-K85.92. This population was divided into two cohorts, those with and without a concomitant diagnosis of COVID-19. Demographic data and patient-characteristics were compared between the acute pancreatitis population with and without a concomitant COVID-19 diagnosis. Severity of hospitalizations were also compared, as defined by mean length of stay, mortality, and complication rates. Complications assessed were pancreatic pseudocyst or pancreatic necrosis, acute kidney failure, diarrhea, sepsis, and respiratory distress. A subgroup analysis was performed to assess the impact of race on hospitalizations with concomitant acute pancreatitis and COVID-19.

Statistical analysis

Data was analyzed using Stata Version 14.1 software (Stata Corp, Texas, USA). In accordance with HCUP guidelines, weights provided by the NIS were used to generate nationally representative estimates. Missing data was excluded. Categorical variables were analyzed using Pearson's chi-squared tests. Continuous variables were analyzed using t-test or Wilcoxon rank-sum test. Multivariate logistic regression was used to assess the independent association of death between those with and without a concomitant COVID-19 diagnosis. Multivariate logistic regression was also used to assess the independent association of race with a concomitant diagnosis of acute pancreatitis and COVID-19.

Results

Patient characteristics

Included were 423,550 weighted inpatient discharges of acute pancreatitis, 2.4% (n=10,075) of which had a concomitant diagnosis of COVID-19 (Supplementary Table 1). A comparison of

patient characteristics between those hospitalized for acute pancreatitis with and without COVID-19 are presented in Supplementary Table 1. Notably, race varied significantly between those without and with COVID-19, particularly among White (63.8% vs 39.0%), Black (16.2% vs 20.9%), and Hispanic (13.6% vs 31.1%) [$\chi^2(5, N=413,495)=661.8, p<0.001$] populations. Expected primary payer and median household income also varied significantly between both cohorts (Supplementary Table 1).

Hospitalization severity

Severity of hospitalizations was evaluated by mean length of stay, complication rate, and inpatient mortality. Mean length of stay was higher in those with concomitant acute pancreatitis and COVID-19 (+5.14 days, $p<0.001$) compared to those without COVID-19 (Supplementary Table 2). Rates of pancreatic pseudocyst and pancreatic necrosis were higher in cohort without COVID-19 (10.8% vs 7.3%) [$\chi^2(1, N=423,550)=25.48, p<0.001$]. However, rates of acute kidney failure, diarrhea, sepsis, and respiratory distress were higher in the COVID-19 cohort (Supplementary Table 2). Death rate was higher in the COVID-19 cohort (2.35% vs 13.5%) [$\chi^2(1, N=423,425)=961.15, p<0.001$]. The adjusted odds of death in the COVID-19 cohort were more than four times greater than the cohort without COVID-19 (aOR=4.24, 95% CI [2.91, 6.18], $p<0.001$) after adjusting for age, race, sex, complications of pancreatitis, and risk factors for developing worsening COVID-19 including hypertension, hyperlipidemia, BMI, and COPD.

Subgroup Analysis of Race

Given significant differences in race distribution between the acute pancreatitis cohorts with and without a concomitant COVID-19 diagnosis, a subgroup analysis was performed to evaluate the effects on race. As noted above, among those with acute pancreatitis, White patients made up 63.8% of the cohort without COVID-19 but only 39.0% of the cohort with COVID-19. While Hispanic patients made up 13.6% of the cohort without COVID-19 but 31.1% of the cohort with COVID-19 [$\chi^2(5, N=413,495)=661.8, p<0.001$] (Supplementary Table 1). The adjusted odds of concomitant acute pancreatitis and COVID-19 in the Hispanic population, as compared to other races, was nearly three times greater after adjusting for age, race, sex, complications of pancreatitis, and risk factors for developing worsening COVID-19 including hypertension, hyperlipidemia, BMI, and COPD (aOR=2.92, 95% CI [2.38, 3.59], $p<0.001$). While severity increased significantly across all races within the COVID-19 cohort, the most significant changes were seen within the Asian and Native American populations (Supplementary Table 2). Mean length of stay in Asians increased by +8.59 days ($p=0.001$) and in Native Americans by +7.21 days ($p=0.005$). Similarly, death increased most in the Asian (3.13% vs 22.40%, $p<0.001$) and Native American (2.44% vs 22.60%, $p<0.001$) populations.

In order to assess whether this disproportionate increase was simply due to an increased proportion of Hispanics being diagnosed with COVID-19, the full 2020 NIS dataset was evaluated. In 2020, those of White race accounted for 66.6% of all-cause diagnoses and 50.9% of COVID-19 diagnoses, Black race accounted for 15.6% of all-cause diagnoses and 19.1% of COVID-19 diagnosis, and Hispanics accounted for 11.3% of all-cause diagnosis and 21.5% of all COVID diagnoses.

Discussion

The 2020 HCUP NIS database was used to characterize the incidence and severity of hospitalizations for acute pancreatitis in those with and without a concomitant diagnosis of COVID-19. Further, disparities were assessed to identify groups disproportionately affected by concomitant acute pancreatitis and COVID-19.

These results demonstrated that patients with concomitant acute pancreatitis and COVID-19 had increased complication rates, mean length of stay, and mortality as compared to those without COVID-19. COVID-19 was an independent risk factor of death in the acute pancreatitis population, with an adjusted odds of death more than four times greater in those with a concomitant diagnosis of COVID-19. These results suggest that those hospitalized with acute pancreatitis should be screened for COVID-19 on admission to prevent delays in initiation of care. Among those with known COVID-19 and acute pancreatitis on admission, both conditions should be aggressively treated to reduce morbidity and mortality rates.

In the subgroup analysis of race, it was found that in those hospitalized with acute pancreatitis, the Hispanic population was disproportionately diagnosed with concomitant COVID-19. The adjusted odds of concomitant acute pancreatitis and COVID-19 diagnoses in the Hispanic population, as compared to other races, was nearly three times greater even after adjusting for known comorbidities of COVID-19. The full 2020 NIS dataset was then evaluated to compare the race distribution among all-cause hospitalizations and those diagnosed with COVID-19. While there was a significant increase in the proportion of Hispanics diagnosed with COVID-19 compared to other all-cause diagnoses (21.5% vs 11.3), the proportion of Hispanics diagnosed with concomitant acute pancreatitis and COVID-19 exceeded this (31.1%). These results indicate that the increased odds of developing concomitant COVID-19 and acute pancreatitis in Hispanics cannot solely be attributed to increased rates of COVID-19 in this population.

While Hispanics were found to have increased rates of diagnosed concomitant acute pancreatitis and COVID-19, the severity of these hospitalizations was greatest in the Asian and Native American populations. While the sample size for these populations was relatively smaller, the results were statistically significant.

There are three hypotheses for the increased incidence of COVID-19 among these minority populations. First, there may be underlying genetic causes that predispose this population to developing acute pancreatitis and COVID-19. There are already known genetic links to developing severe COVID-19 pneumonia with mutations found in type I interferons [7]. The cellular mechanisms for acute pancreatitis in the setting of COVID-19 are still being explored and could expose a genetic link explaining why the Hispanic population was more susceptible to developing concomitant COVID-19 and acute pancreatitis and the Asian and Native American populations were more susceptible to increased morbidity and mortality.

Second, it is known that patients with metabolic syndrome have a higher incidence of morbidity and mortality related to

both COVID-19 and acute pancreatitis [8-10]. While certain metabolic comorbidities associated with COVID-19 were controlled for, it is still possible that the high rates of metabolic syndrome in the Hispanic and Native American populations influenced the risk of concomitant acute pancreatitis and COVID-19 [11] [12]. Further, the Hispanic and Asian populations have the fastest growing prevalence of metabolic syndrome in the United States [12].

Third, healthcare inequities and social determinants of health are likely contributing to these racial disparities. Hispanics make up 18% of the United States population and nearly 20% of this population is uninsured, in comparison to less than 5% of the non-Hispanic white population [13]. While nearly 22% of the Native Americans are uninsured [14]. Prior to the pandemic 24% of Native Americans and 19% of Hispanics fell under the poverty line compared to 9% of White Americans [14]. While insurance and income were controlled for in the multivariate logistic regression, it was not possible to control for all social determinants of health including access to high quality preventative care, reliable medical information, healthful foods, secure housing, and transportation.

These results suggest that primary prevention should be directed toward both the Hispanic population, as incidence was most increased in this group, and the Asian and Native American populations, as severity was most increased in these groups. To improve primary prevention, structural changes to the way primary care is delivered must be implemented such that equity in quality and access to care is improved. Not only does access to quality care need to increase, but targeted efforts to make medical education and vaccines accessible are necessary. Further, targeted policy changes that address disparities in social determinants of health are necessary.

Study Strengths and Limitations

While the HCUP NIS is a unique resource that allows for the calculation of nationally representative estimates, there are inherent limitations to using a claims database. First, each observation in the HCUP NIS represents a single inpatient stay. Thus, the data is limited to only those who seek care in the hospital. Further, this does not allow for the longitudinal assessment of patients, therefore only events during a given hospitalization can be assessed. Second, the HCUP NIS is a claims database that relies on reported ICD-10-CM codes. Thus, the analysis depends on the reliability of these classifications. Further, this format does not allow for detailed individual level data regarding lab results or imaging that would help to understand the patient's clinical condition at a more granular level. Finally, it is not possible to differentiate the chronicity of the diagnoses, for example whether COVID-19 and acute pancreatitis were diagnosed concurrently or if COVID-19 was a precursor to developing acute pancreatitis. More detailed information about patients' social history could also allow for a greater understanding of the health disparities noted in this analysis. Lastly, COVID-19 data is currently limited to the 2020 dataset of the HCUP NIS.

Opportunities for Future Research

As more data on COVID-19 is released, further evaluation can be done to see how the trends noted in this analysis changed

or persisted over time. Further, while this analysis demonstrates clear racial disparities, it is unclear why these disparities exist. Further exploration of genetic factors, comorbidities, and social determinants of health is required.

Conclusions

In conclusion, patients admitted with concomitant COVID-19 and acute pancreatitis should be aggressively treated to reduce morbidity and mortality. Increased efforts at COVID-19 primary prevention should be directed toward both the Hispanic population, as incidence was most increased in this group, and Asian and Native American populations, as severity was most increased in these groups. Further research needs to be done to determine the underlying cause of these racial disparities.

Abbreviations

COVID-19: Coronavirus disease pandemic; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; ACE2 Angiotensin-converting enzyme 2 receptor; HCUP: Healthcare Cost and Utilization Project; NIS: National Inpatient Sample; ICD-10-CM: International Classification of Diseases Tenth Revision Clinical Modification; aOR: Adjusted odds ratio

Conflict of interest

We do not have any financial or non-financial conflicts of interest.

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