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# Impact of COVID-19 pandemic on acute pancreatitis presentations, management, and in-hospital outcomes: a single-center, retrospective observational study from the northeast of China

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***Abstract***

**Background:** Since initially detected in late December 2019, the novel coronavirus disease 2019 (COVID-19) outbreak rapidly swept the world, which has profoundly affected healthcare system and clinical practice in the management of gastrointestinal diseases.

**Objectives:** We aimed to evaluate the impact of COVID-19 pandemic on the pattern of hospital admissions and healthcare services for acute pancreatitis (AP).

**Design:** We conducted a retrospective observational cohort study using the anonymized electronic medical records.

**Methods:** This single-center, retrospective observational study from a regional medical center in the northeast of China included all consecutively admitted patients with AP from 23 January to 10 June 2020 (during the COVID-19 outbreak in Harbin), compared with the equivalent period of the previous year, in terms of demographics, clinical characteristics, and in-hospital outcomes.

**Results:** In this article, we observed a reduction in AP admissions after the beginning of COVID-19 outbreak. With the prolonged time from symptom onset to hospitalization [32.0 (22.0–72.0) *versus* 18.0 (12.0–24.0) h; $p < 0.001$], a higher proportion of AP patients developed acute renal failure (14.0% *versus* 7.4%, $p = 0.004$) and acute necrotic collection (16.5% *versus* 11.2%; $p = 0.038$) in the COVID-19 era. The percentage of alcohol etiology significantly decreased after the implementation of social restriction measures (11.5% *versus* 20.4%; $p = 0.002$), whereas biliary etiology was numerically more common amidst the COVID-19 era (41.6% *versus* 32.6%; $p = 0.014$). No significant differences were found in the rates of intensive care unit admission and mortality between the two groups.

**Conclusion:** This study preliminarily demonstrated the descending trend and delay in hospital presentations for AP during the outbreak of COVID-19. Given that the pandemic may persist for several years, adjustments of medical services according to the varying degrees of local breakouts are imperative to provide appropriate care for AP patients and diminish the risk of viral transmission.

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***Keywords:*** acute pancreatitis, coronavirus disease 2019, pandemic

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## Introduction

Acute pancreatitis (AP) is one of the most frequent reasons for gastrointestinal-related hospital presentation with an unpredictable clinical course.[1] Although the majority of patients with self-limited edematous pancreatitis usually recover within several days, around 20% will progress to infected (peri-)pancreatic necrosis and/or organ failure, resulting in substantially higher mortality rates of 20–43%.[2] The management paradigms of AP have developed into tailor-made, multidisciplinary approaches provided by specialists in gastroenterology, (interventional) radiology, surgery, nutrition, emergency and critical care medicine.[3] Once the patient arrives at the emergency room, accurate diagnosis, and early supportive therapies, including fluid balance, analgesia, and nutritional support, could effectively ameliorate tissue hypoperfusion and hyperinflammation.[4,5] In the subacute stage, timely recognition of infectious complications and reversible causes of AP is essential to prevent disease progression or recurrence.[6]

Since its discovery in late 2019, the coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been rapidly gripping the world, which created unprecedented healthcare and socioeconomic challenges globally.[7] After the implementation of social distancing and lockdown policies to restrict viral spread, changing patterns of hospital admissions were observed in other acute disorders.[8,9] Moreover, relocation of medical resources for COVID-19 and fear of acquiring SARS-CoV-2 infection in hospital setting could also affect patients access to timely treatment.[10] In addition, there has been interest in the possible association between SARS-CoV-2 infection and AP, given the fact that angiotensin-converting enzyme 2 (ACE2) receptors and transmembrane protease serine 2 are also highly expressed in pancreatic ductal and islet cells.[11]

The impact of dynamic zero COVID-19 policy on etiology and management of AP patients is still unclear. Herein, we conducted an observational study to evaluate the hospital admissions, etiologies, complications, and clinical outcomes of consecutive AP patients admitted following the COVID-19 outbreak in Harbin and compare them with those who presented during corresponding period outside the pandemic time window.

## Methods

### *Study periods and population*

This retrospective study included all consecutive AP patients meeting the revised Atlanta criteria[12] admitted to the First Affiliated Hospital of Harbin Medical University (1stHMU) and Qunli Branch Hospital (QBH) from 23 January 2020 (the first case of COVID-19 in Harbin was confirmed and a nationwide first-level public health emergency response mechanism initiated) to 10 June 2020 (the emergency response to COVID-19 was lowered into the third level in Harbin),[13] which defined as the COVID-19 era group, compared with the corresponding period in 2019 (23 January to 10 June, defined as the control group). During the early phase of the pandemic, 1stHMU was selected as the major tertiary referral center for acute and critical care, and QBH was converted into specialized treatment center for novel coronavirus patients in Heilongjiang, which provided us with an opportunity to observe the impact of COVID-19 pandemic on AP patients. All data supporting this study were obtained from the retrieval of electronic health records of unselected patients hospitalized for AP in our center based on the International Classification of Diseases, 10th Edition. Exclusion criteria included the presentations for chronic pancreatitis, and if the patients had been admitted for AP more than one time during the study period, only the last episode of admission was eligible. Consecutive patients who fulfilled all of the inclusion criteria and none of the exclusion criteria were admitted to this study. This retrospective and observational designed study did not provide additional intervention on included patients. Ethical approval was obtained from the Ethics Committee of 1stHMU, Harbin 150081, China, with the following reference number IRB-AF/SC-04/02.0 and Chinese Clinical Trial Registry number ChiCTR2100043350. This study was performed in accordance with the Declaration of Helsinki and written informed consent has been granted a waiver from ethical review board as we solely extracted anonymized data retrospectively without any protected information. Each patient enrolled in this study was assigned a unique de-identified number, and all anonymous patient data were recorded, identified, and analyzed in relation to this de-identified number. The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[14] Details regarding COVID-19 prevalence in Harbin

and reorganization of our center during the study period are provided in Supplemental Materials.

### *Data collection*

All clinical data were collected by screening the electronic medical system of our center. The primary objective was to assess the incidence of AP-related hospitalization, time from initial symptoms onset to first medical contact, and all-cause mortality. Secondary outcomes including changes in demographic and clinical characteristics, and conventional management of patients with AP. Specifically, clinical features included the Bedside Index for Severity in AP (BISAP) score, rate of local or systematic complications, total hospital length of stay (LOS), and intensive care unit (ICU) admission rate. The therapeutic approaches predominantly included conservative management (i.e. medical treatment without any invasive procedures), mechanical respiratory/renal/circulatory support, percutaneous catheter drainage (PCD) or endoscopic transmural drainage, minimally invasive necrosectomy, open pancreatic debridement (OPD), percutaneous transperitoneal gallbladder drainage, endoscopic retrograde cholangiography (ERCP) with endoscopic sphincterotomy or endoscopic nasobiliary drainage, cholecystectomy, etc.

### *Study definitions*

Accurate diagnosis of AP was made when two or more of the following criteria were fulfilled: (1) typical abdominal pain; (2) elevated serum amylase or lipase levels at least threefold the upper limit of normal; and (3) imaging features consistent with the signs of AP on transabdominal ultrasonography, computed tomography, or magnetic resonance imaging. Local or systematic complications were categorized based on the revised Atlanta criteria, evaluated by two independent physicians.[12] The standards to define the most probable etiologies were provided in the Supplemental Materials.

### *Statistical analysis*

Descriptive statistics for continuous variables were described as mean ± standard deviation or median (interquartile range) according to variable distributions and analyzed with Student's t-test or Mann–Whitney U-test. Categorical variables were reported as frequencies (percentages) and analyzed with Pearson's $\chi^2$ test or Fisher's exact test. A two-sided $p < 0.05$ was considered statistically significant, and Bonferroni correction was applied to correct for multiple comparisons whenever appropriate. For the primary outcome, incidence rates (IRs) of AP were estimated by dividing the number of cumulative AP-related hospitalizations by the number of weeks for each time period. Poisson regression approach was used to verify the impact of COVID-19 on the weekly number of AP-related admissions and the calculated result was denoted by the incidence rate ratio (IRR).[9] Statistical analyses were performed using IBM-Statistical Package for the Social Sciences for Windows software version 25 (SPSS Inc., Chicago, IL, USA) and R software version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

During the study period, a total of 736 patients with AP were included in this analysis. Among them, 279 patients were admitted during the COVID-19 period, accounting for a mean of 14 admissions/week. In all, 457 patients were admitted for AP during the equivalent period in 2019, accounting for a mean of 23 admissions/week. Since the COVID-19 outbreak in Harbin, we observed a reduction of weekly AP admissions in the COVID-19 era (Figure 1), especially after the initiation of public health emergency response, followed by gradually returning to the normal level until the end of this study. The IR in the COVID-19 era was lower when compared with the pre-pandemic period [IRR: 0.61, 95% confidence interval (CI): 0.55–0.68; $p < .001$). IRR for different AP etiologies were as follows: acute gallstone pancreatitis (AGP; IRR: 0.78, 95% CI 0.7–0.87; $p = 0.049$); acute alcohol pancreatitis (IRR: 0.32, 95% CI: 0.29–0.36; $p < 0.001$); idiopathic AP (IRR: 0.65, 95% CI: 0.59–0.72; $p = 0.004$).

### *Baseline demographic and clinical characteristics*

The median age of AP patients included in this study was 46 (35–61) years and 181 (64.9%) of them were males, with a mean body mass index of 25.3 ± 3.8 kg/m$^2$ and median serum triglyceride (TG) level of 2.62 (1.71–5.47) mmol/L. Demographic characteristics and serum TG were similar between the two groups as shown in Table 1.

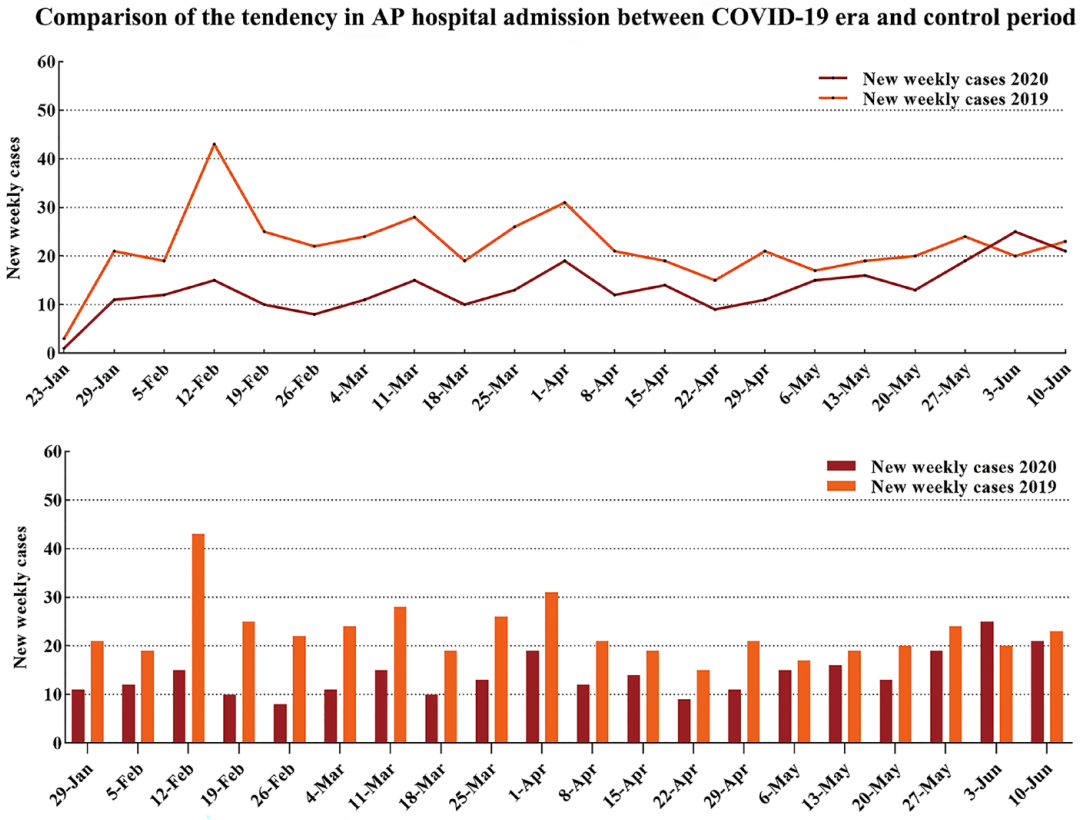


**Figure 1.** Comparison of the tendency in hospital admissions for AP between the COVID-19 era (crimson line/columns) and control period (orange line/columns). Weekly AP admissions were decreased by a factor of 39% (95% CI: 32%–45%, according to IRR of Poisson regression) since the initiation of public health emergency response, followed by gradually returning to the normal level until the end of the COVID-19 outbreak in Harbin.
AP, acute pancreatitis; CI, confidence interval; COVID-19, coronavirus 2019; IRR, incidence rate ratio.

Since the onset of COVID-19 outbreak, we observed a significantly prolonged time from the onset of AP-related symptoms to first medical contact as compared to the pre-pandemic period [32.0 (22.0–72.0) *versus* 18.0 (12.0–24.0) h; $p < 0.001$; Figure 2]. The percentage of patients transferred from primary hospitals was similar between two periods (11.8% *versus* 9.0%; $p = 0.211$), and the rate of hospital readmission was nominally increased in the COVID-19 era group (18.3% *versus* 13.6%; $p = 0.085$), as a consequence of residual infected necrotic collections or relapse.

### *Patterns of etiology*

Cholelithiasis was the predominant etiology in both groups. Biliary etiology was more common in the COVID-19 era group compared with control group (41.6% *versus* 32.6%; $p = 0.014$; Figure 3), although not statistically significant after Bonferroni correction. As the second leading etiology, alcohol abuse was more frequent in the pre-pandemic period at 20.4%, compared to 11.5% in the COVID-19 period ($p = 0.002$). There was no significant difference in other etiologies between groups. As for infectious etiology, in the COVID-19 era group 2 patients (0.4%) with AP were etiologically related to cytomegalovirus and Epstein-Barr virus (EBV), respectively, compared with three cases (0.7%) in the control group related to EBV or mumps virus infection. Furthermore, two patients with unknown etiology and coexistent SARS-CoV-2 infection in the COVID-19 era group were transferred to Qunli branch hospital for isolated treatment.

### *Disease severity and clinical complications*

As shown in Table 2, the BISAP score was significantly higher in the COVID-19 era group, with

**Table 1.** Comparison of baseline characteristics and etiologies of patients admitted for AP between COVID-19 period and control period.

| Characteristics | Overall ($n=736$) | COVID-19 period ($n=279$) | Control period ($n=457$) | $p$ Value |
|---|---|---|---|---|
| Age, years | 45 (34–59.5) | 46 (35–61) | 44 (34–59) | 0.497 |
| Male sex, no. (%) | 478 (64.9%) | 181 (64.9%) | 297 (65%) | 0.975 |
| BMI, kg/m$^2$ | 25.2 ± 3.6 | 25.3 ± 3.8 | 25.2 ± 3.4 | 0.675 |
| Serum TG, mmol/L | 2.87 (1.76–5.35) | 2.62 (1.71–5.47) | 2.93 (1.82–5.30) | 0.359 |
| Time to first medical contact, hours | 24.0 (12.0–36.0) | 32.0 (22.0–72.0) | 18.0 (12.0–24.0) | <0.001* |
| Transferred from other hospital, no. (%) | 74 (10.1%) | 33 (11.8%) | 41 (9.0%) | 0.211 |
| Hospital readmission, no. (%) | 113 (15.4%) | 51 (18.3%) | 62 (13.6%) | 0.085 |
| Etiology, no. (%) | | | | 0.038 |
| Gallstones | 265 (36.0%) | 116 (41.6%) | 149 (32.6%) | 0.014 |
| Alcohol | 121 (16.4%) | 32 (11.5%) | 93 (20.4%) | 0.002* |
| Metabolic (hypertriglyceridemia) | 84 (11.4%) | 25 (9.0%) | 59 (12.9%) | 0.102 |
| Autoimmune | 12 (1.6%) | 5 (1.8%) | 7 (1.5%) | 0.773 |
| Drug induced | 4 (0.5%) | 1 (0.4%) | 3 (0.7%) | † |
| Operation/trauma related | 7 (1.0%) | 3 (1.1%) | 4 (0.9%) | † |
| ERCP related | 4 (0.5%) | 1 (0.4%) | 3 (0.7%) | † |
| Infectious etiology | 5 (0.7%) | 2 (0.7%) | 3 (0.7%) | † |
| Tumor related | 6 (0.8%) | 4 (1.4%) | 2 (0.4%) | 0.207 |
| Mixed etiology | 39 (5.3%) | 14 (5.0%) | 21 (4.6%) | 0.794 |
| Idiopathic | 189 (25.7) | 76 (27.2%) | 113 (24.7%) | 0.449 |

Summary statistics were expressed as number (%) for categorical variables and mean ± SD, median (interquartile range) for continuous variables. A two-sided $p$ value of less than 0.05 was considered statistically significant (*).
†It indicates insufficient number of cases to enable formal comparison of etiologic frequency.
AP, acute pancreatitis; BMI, body mass index (weight in kilograms divided by height in meters squared); COVID-19, the novel coronavirus disease 2019; ERCP, endoscopic retrograde cholangiography; TG, triglyceride.

16.8% having a score greater than 2, as compared to 11.4% in the control group ($p=0.035$). Of the 736 patients hospitalized for AP in this study, mild AP (MAP) was less frequent in the COVID-19 era group compared to control group (45.2% *versus* 52.5%; $p=0.053$). In parallel, 42.3% and 38.7% of patients in the COVID-19 era and control groups were diagnosed with moderately severe AP (MSAP), respectively ($p=0.339$). There was a trend, although not statistically different, for patients admitted with AP during the COVID-19 pandemic to have a higher proportion of progressing to severe disease as compared with control group (12.5% *versus* 8.8%; $p=0.099$), and most of them were referred from primary hospitals.

Comparison of local complications showed that patients in the COVID-19 era group were more likely to develop acute necrotic collection (ANC, 16.5% *versus* 11.2%; $p=0.038$) as compared to control group. Moreover, the occurrence of systemic complications was also higher in AP patients admitted during the pandemic. Among them, 39 (14.0%) patients in the COVID-19 era

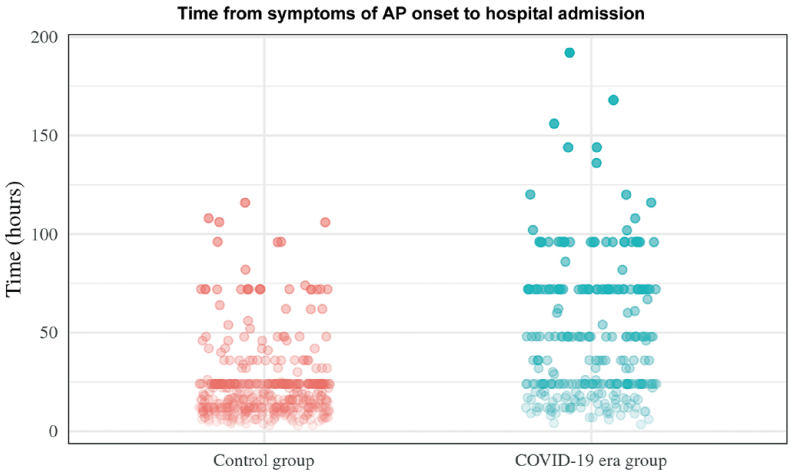


**Figure 2.** Time from AP-related symptoms onset to hospital admission between the two groups. Time from the onset of AP-related symptoms to hospital admission was significantly prolonged in the COVID-19 era (cyan bubbles) as compared to control period (orange bubbles). The median times and interquartile range were 32.0 (22.0–72.0) and 18.0 (12.0–24.0) hours for the COVID-19 period compared to the control period, respectively ($p < 0.001$).
AP, acute pancreatitis; COVID-19, coronavirus 2019.

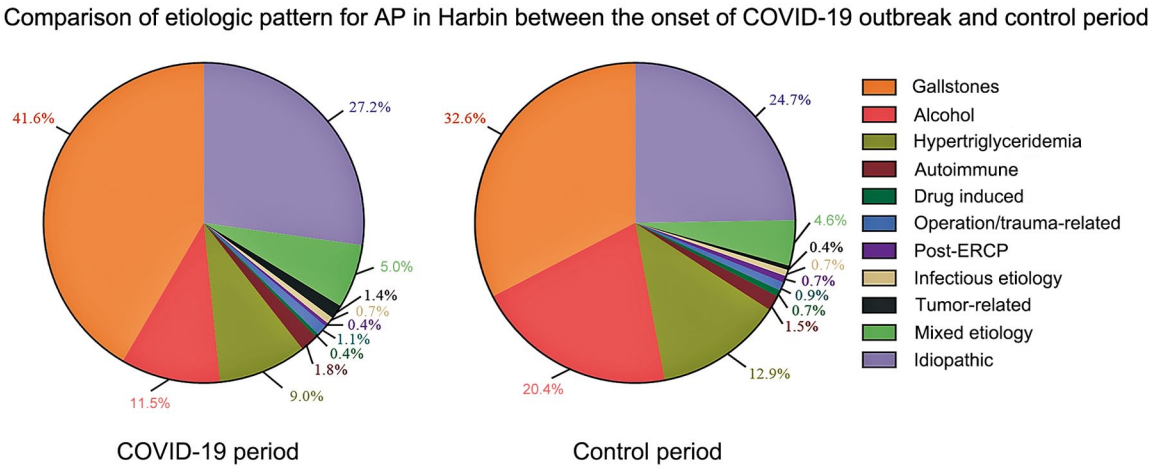


**Figure 3.** Impact of COVID-19 outbreak on etiologic pattern for AP. Gallstones were the predominant etiology of AP (41.6%), followed by idiopathic pancreatitis (27.2%) and alcoholic pancreatitis (11.5%) during COVID-19 period. The percentage of alcohol etiology significantly decreased after the COVID-19 outbreak.
AP, acute pancreatitis; COVID-19, coronavirus 2019.

group and 34 (7.4%) patients in the control group developed acute renal failure (ARF, $p = 0.004$), and numerically higher rates of acute respiratory distress syndrome (ARDS, 8.6% *versus* 6.3%, $p = 0.251$) and sepsis (4.7% *versus* 2.4%, $p = 0.095$) were observed in the COVID-19 era group.

### *Management and in-hospital outcomes*

The proportion of patients who received respiratory or circulatory supports was similar between two groups, whereas the percentage of patients receiving mechanical renal replacement therapy in the COVID-19 era group was higher than control group (12.2% *versus* 6.8%; $p = 0.012$).

**Table 2.** Comparison of complications, treatment approaches and in-hospital outcomes of patients admitted for AP between COVID-19 period and control period.

| Characteristics | Overall (*n* = 736) | COVID-19 period (*n* = 279) | Control period (*n* = 457) | *p* Value |
|---|---|---|---|---|
| BISAP score, no. (%) | | | | 0.035 |
| ⩽2 | 637 (86.5%) | 232 (83.2%) | 405 (88.6%) | |
| <2 | 99 (13.5%) | 47 (16.8%) | 52 (11.4%) | |
| Severity, no. (%) | | | | 0.087 |
| Mild | 366 (49.7%) | 126 (45.2%) | 240 (52.5%) | 0.053 |
| Moderate | 295 (40.1%) | 118 (42.3%) | 177 (38.7%) | 0.339 |
| Severe | 75 (10.2%) | 35 (12.5%) | 40 (8.8%) | 0.099 |
| Complications, no. (%) | | | | |
| APFC | 262 (35.6%) | 104 (37.3%) | 158 (34.6%) | 0.458 |
| ANC | 97 (13.2%) | 46 (16.5%) | 51 (11.2%) | 0.038* |
| Pancreatic pseudocyst | 18 (2.4%) | 8 (2.9%) | 10 (2.2%) | 0.563 |
| WON | 6 (0.8%) | 4 (1.4%) | 2 (0.4%) | 0.207 |
| Thrombotic events | 9 (1.2%) | 4 (1.4%) | 5 (1.1%) | 0.736 |
| Pancreatic portal hypertension | 6 (0.8%) | 4 (1.4%) | 2 (0.4%) | 0.207 |
| IAH or GIH | 7 (1.0%) | 3 (1.1%) | 4 (0.9%) | † |
| Enteric fistula | 4 (0.5%) | 2 (0.7%) | 2 (0.4%) | 0.636 |
| ARF | 73 (9.9%) | 39 (14.0%) | 34 (7.4%) | 0.004* |
| ARDS | 53 (7.2%) | 24 (8.6%) | 29 (6.3%) | 0.251 |
| Cardiovascular failure | 33 (4.5%) | 15 (5.4%) | 18 (3.9%) | 0.361 |
| DIC | 5 (0.7%) | 2 (0.7%) | 3 (0.7%) | † |
| ACS | 7 (1.0%) | 5 (1.8%) | 2 (0.4%) | 0.111 |
| Sepsis | 24 (3.3%) | 13 (4.7%) | 11 (2.4%) | 0.095 |
| Treatment approaches, no. (%) | | | | |
| Conservative treatment | 537 (73.0%) | 195 (69.9%) | 342 (74.8%) | 0.143 |
| PCD/ETD | 78 (10.6%) | 42 (15.1%) | 36 (7.9%) | 0.002* |
| Minimally invasive debridement | 21 (2.9%) | 8 (2.9%) | 13 (2.8%) | 0.986 |
| Open necrosectomy | 16 (2.2%) | 4 (1.4%) | 12 (2.6%) | 0.282 |
| Cholecystectomy | 52 (7.1%) | 9 (3.2%) | 43 (9.4%) | 0.001* |
| PTGD | 11 (1.5%) | 5 (1.8%) | 6 (1.3%) | 0.756 |
| ERCP ± EST/ENBD | 40 (5.4%) | 19 (6.8%) | 21 (4.6%) | 0.198 |

*(Continued)*

**Table 2.** (Continued)

| Characteristics | Overall ($n=736$) | COVID-19 period ($n=279$) | Control period ($n=457$) | $p$ Value |
|---|---|---|---|---|
| Nasogastric or nasojejunal feeding | 61 (8.3%) | 24 (8.6%) | 37 (8.1%) | 0.809 |
| Invasive mechanical ventilation | 44 (6.0%) | 18 (6.5%) | 26 (5.7%) | 0.672 |
| Renal replacement therapy | 65 (8.8%) | 34 (12.2%) | 31 (6.8%) | 0.012* |
| Circulatory support | 40 (5.4%) | 17 (6.1%) | 23 (5.0%) | 0.538 |
| ICU admission, no. (%) | 80 (10.9%) | 31 (11.1%) | 49 (10.7%) | 0.869 |
| Length of Hospital Stay, day | 9 (6–13) | 8 (6–12) | 9 (6–13) | 0.023* |
| In-hospital mortality, no. (%) | 14 (1.9%) | 5 (1.8%) | 9 (2.0%) | 0.864 |

Summary statistics were expressed as number (%) for categorical variables and mean ± SD, median (interquartile range) for continuous variables. A two-sided $p$ value of less than 0.05 was considered statistically significant (*).
†It indicates insufficient number of cases to enable formal comparison of etiologic frequency.
ACS, abdominal compartment syndrome; ANC, acute necrotic collection; APFC, acute peripancreatic fluid collection; ARDS, acute respiratory distress syndrome; ARF, acute renal failure; BISAP, bedside index of severity in pancreatitis; DIC, disseminated intravascular coagulation; ENBD, endoscopic nasobiliary drainage; EST, endoscopic sphincterotomy; ERCP, endoscopic retrograde cholangiography; ETD, endoscopic transmural drainage; GIH, gastrointestinal hemorrhage; IAH, intra-abdominal hemorrhage; ICU: intensive care unit; PCD: percutaneous catheter drainage; PTGD, percutaneous transperitoneal gallbladder drainage; WON, walled-off necrosis.

Drainage of pancreatic necrosis was performed in 42 patients (15.1%) in the COVID-19 era group, compared with 36 patients (7.9%) in the control group ($p=0.002$), for infected necrosis or obstructive complications. Alternatively, in the pandemic period, 12 patients (4.3%) underwent minimal invasive or open necrosectomy for deterioration of infection symptoms as compared with 25 patients (5.5%) in the control group ($p=0.49$). Regarding to patients with AGP, the proportion of same-admission cholecystectomy significantly declined in the COVID-19 era group compared with the control group (3.2% *versus* 9.4%; $p=0.001$). ERCP procedures were performed in 6.8% AGP for persisting biliary obstruction or cholangitis during the pandemic, compared with 4.6% in the control period ($p=0.198$).

There were no significant differences in the rates of ICU admission and in-hospital mortality between the two groups. Among those with idiopathic AP, two patients (0.7%) concomitant with SARS-CoV-2 infection were admitted to the isolation ICU and recovered uneventfully after supportive therapy. The total in-hospital stay was shorter in the COVID-19 era group [8 (6–12) *versus* 9 (6–13) days; $p=0.023$].

## Discussion

The outbreak of COVID-19 has profoundly affected healthcare systems and the management of other gastrointestinal emergencies. In this study, we observed a substantial reduction in AP admissions coincident with the activation of public health emergency response, followed by gradually returning to normal level until the end of the first-wave epidemic in Harbin, and time from the onset of AP-related symptoms to hospital presentation was significantly lengthened during the pandemic compared with the same period of previous year. It was conceivable that patients avoided in-hospital visits and emergency medical services due to fear of catching SARS-CoV-2 infection during the pandemic, which was associated with their lack of awareness regarding the disease severity and viral transmission modes.[10] Furthermore, the burden of epidemic prevention and stringent pre-hospital quarantine measures including SARS-CoV-2 nucleic acid testing and chest computed tomography examination could also contribute to delaying presenting to hospital and reduce the efficiency of medical care. In addition, people were advised to stay at home for an extended Spring Festival, which potentially restricted unhealthy dietary habits including alcohol abuse and reduced the risk of AP episodes.

Delaying presentation of AP patients might prevent timely fluid resuscitation and other supportive treatment, which were essential in the early stage to ameliorate tissue hypoperfusion and hypoxia. It has been reported that early goal-directed hydration within the initial 24 h could improve the clinical outcomes of patients with predicted SAP.[4] In our study, an increased incidence of ARF during hospitalization was observed in the COVID-19 era group, which might result from deferred fluid resuscitation and circulatory hypovolemia-related renal ischemia/reperfusion injury.[15] Correspondingly, more patients underwent kidney replacement therapy during the pandemic to alleviate severe hyperkalemia, metabolic acidemia, or pulmonary edema. The delay in time to admission may also impact anti-inflammatory treatments and increase the risks of ARDS and other systemic complications, although we observed no significant difference. Both patients tested positive for SARS-CoV-2 deteriorated into ARDS in our study. Nonetheless, 75% of AP patients with ARDS in the COVID-19 era group received mechanical ventilation compared with 89.7% in the control group, which may be associated with altered airway management patterns during the pandemic to reduce aerosol generation. Specifically, a proportion of patients with mild ARDS recovered from the treatment of high-flow nasal oxygen or non-invasive positive pressure ventilation, and alternatively, endotracheal intubation would be implemented if no stabilization in oxygen saturation was achieved within 1–2 h.

At the beginning of the first-wave pandemic, SARS-CoV-2 infection was considered to manifest predominantly as fever and other respiratory symptoms, whereas increasing evidence suggests that up to 14% COVID-19 patients presented with gastrointestinal symptoms as their initial symptoms.[16] Therefore, more attention should be paid to differential diagnosis of potential SARS-CoV-2 infection when patients presented with abdominal pain and hyperamylasemia during regional COVID-19 outbreaks.[17] Given that ACE2 receptor is also expressed in gastrointestinal tract including pancreas, the associations between pancreatitis and COVID-19 need to be further explored. El-Kurdi et al. speculated that SARS-CoV-2 might promote the leakage of TG lipase into visceral adipose tissue by targeting adipocytes and pancreatic cells, which could induce unsaturated fatty acids generation and mediated lipotoxic organ failure.[18] In the clinical context, several retrospective studies have reported individuals with pre-existing pancreatitis shown more susceptibility to SARS-CoV-2 infection,[19] while patients with concomitant COVID-19 were at increased risk of progressing to moderate or severe AP.[20] Consistent with the previous study by Inamdar et al.,[17] our study also implicated hospitalized patients with concomitant SARS-CoV-2 infection and AP had increased requirements for mechanical ventilation and prolonged ICU stay. To further investigate the associations between SARS-CoV-2 infection and pancreatitis, we simultaneously collected clinical data of 145 consecutive patients hospitalized with COVID-19 in QBH during the study period. We observed similar patterns cytokine elevations in severe COVID-19 and AP (as shown in Supplemental material). Previous studies have shown interleukin (IL)6, IL10, and tumor necrosis factor alpha were involved in the inflammatory processes of COVID-19 and AP.[18] Conceivably, pre-activation of immune microenvironment in AP patients might increase the likelihood of amplified inflammatory cytokine storm when concomitant SARS-CoV-2 infection occurs, and the detailed mechanism requires further in-depth studies investigation, which would be helpful for the development of more effective strategies to improve outcomes in both inflammatory diseases.[21]

This study also showed the incidence of ANC significantly increased in the COVID-19 era group, which was probably associated with late presentation and inappropriate management of AP patients in the early phase of the pandemic. Nevertheless, we observed a downward trend of patients receiving surgical treatment, accompanied by increased frequency of ultrasound-guided PCD for infectious necrosis, reflecting impact of the pandemic on conventional activities of surgical units, such as limiting the number of operations, rescheduling priorities, and enforcing cross-infection control measures. During the COVID-19 pandemic, endoscopic or operative therapies might become high-risk procedures for patients with SARS-CoV-2 positive or uncertain status on account of the possibility of exposure to aerosol of respiratory and digestive tract secretions.[22] Therefore, PCD procedure under protective equipment might potentially reduce the risk of nosocomial SARS-CoV-2 transmission and laparotomy would be reserved for AP patients with fatal complications.

During the first-wave COVID-19 outbreak in Harbin, we observed alcohol etiology accounted for a declined proportion of hospitalized AP cases. The reasons underlying this alteration were multifactorial and likely ascribed to implication of social distancing policy, including suspension of public gatherings, closure of restaurants and pubs, which unintentionally promoted a healthier diet without binge eating and alcohol abuse. The proportion of biliary etiology tended to be higher in the COVID-19 era over control period, while AGP patients undergoing same-admission cholecystectomy substantially reduced. Although the rehospitalization rate was numerically higher in the COVID-19 era group, no statistically significant difference was identified, which may be related to the relatively short study period. These findings were consistent with results of a recently study from United Kingdom,[23] which reported the COVID-19 pandemic reducing access to cholecystectomy in eligible AGP patients and potentially driven the increased risk of AP recurrence and readmission.[24] In this context, the risk and benefits of index cholecystectomy should be reassessed according to clinical condition of AGP patients and stratification of SARS-CoV-2 transmission risk in endemic areas.

Current study data showed the proportion of SAP tended to increase, accompanied by a declining tendency of MAP during the early phase of COVID-19 pandemic. Reassuringly, ICU admission rate and in-hospital mortality were similar between the two periods in our center, suggesting appropriate adjustment of practical strategies might be useful for effective treatment of AP in response to COVID-19 outbreak. Alternatively, the median LOS tended to be shorter in the COVID-19 era, reflecting the impacts of the pandemic on management of hospitalized AP patients. Specifically, to cope with the restricted number of available beds and diverted medical resources for COVID-19, patients with AP were often stabilized, recovered, and discharged directly or re-presented to the primary hospitals to ensure a relatively rapid in-patient turnover, and appropriate follow-up of these patients would be conducted remotely with the help of telehealth technology.

To address ongoing medical needs during the pandemic, our department optimize telemedicine service to provide medical care remotely for the most people with mild or chronic disease possible as the substitute of in-person visits and forwarding triage. In addition, the program ensures remote physicians promptly organize patients with progressive disease to attend the nearest medical institutions and schedule face-to-face examinations.[25] For patients requiring urgent surgical treatment, pre-hospital risk stratification might enable timely clinical interventions and protecting healthcare workers and vulnerable pancreatic diseases patients from the risk of nosocomial COVID-19 infection. As new variants of SARS-CoV-2 constantly emerge, the rate of Omicron sub-variants spread much faster than earlier strains of the coronavirus and it remains unclear how long the pandemic will persist.[26] In this context, telemedicine might help to minimize the impact of delayed medical care and diminish adverse clinical outcomes of AP patients under the premise of proper application.[27]

Several factors limit the interpretation of the study findings. Considering the characteristics of retrospective observational study design, which precludes robust causal inference, our study findings cannot draw any definitive conclusions on the effectiveness of treatment modalities and long-term consequences of AP patients during the pandemic. Prospective follow-up study would be a superior way to evaluate the long-term ramifications of COVID-19 pandemic on patients with AP. Furthermore, individual data collected through electronic medical system were too limited to analyze the direct impacts of concomitant SARS-CoV-2 infection on clinical trajectory of AP patients. Nonetheless, the current report provided an important insight into the possible effect of present pandemic on hospitalization and management of AP patients.

## Conclusion

In conclusion, our data have shown the descending trend and delay in hospital admissions of AP patients since the outbreak of COVID-19, accompanied by higher prevalence of ANC and systemic complications. Social distancing and public anxiety have potentially contributed to medical-seeking behavior change, and the current pandemic necessitated reorganization of medical centers to optimally balance the needs of patients with gastrointestinal emergencies and containment of viral transmission according to the status of local breakouts. The impact of COVID-19 outbreak and reshaping of first-aid strategies on the

long-term clinical outcomes of AP patients requires further investigation.

## Declarations

### *Ethics approval and consent to participate*

This retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Harbin Medical University, Harbin 150081, Heilongjiang Province, China, with the following reference number IRB-AF/SC-04/02.0. and written informed consent has been granted a waiver from ethical review board as this study solely extracted anonymized data retrospectively.

### *Consent for publication*

All the authors reviewed, edited, and approved the final manuscript and made the decision to submit the manuscript for publication.

### *Author contribution(s)*

**Zu-Chao Du:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Validation; Visualization; Writing – original draft; Writing – review & editing.

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**Bei Sun:** Conceptualization; Data curation; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing – review & editing.

**Jian Zhang:** Data curation; Formal analysis; Investigation; Methodology; Resources; Validation; Writing – original draft.

**Xin-Jian Li:** Conceptualization; Data curation; Investigation; Methodology; Software; Validation; Visualization; Writing – original draft.

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### *Competing interests*

The authors declare that there is no conflict of interest.

### *Availability of data and materials*

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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## Supplemental material

Supplemental material for this article is available online.

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