Clinical Characteristics and Short-term Outcomes of Acute Pancreatitis with COVID-19

Jinchang Zhang
The Affiliated Hospital of Southwest Medical University
De luo
The Affiliated Hospital of Southwest Medical University
Maoji kang
The Affiliated Hospital of Southwest Medical University
Bo Li
The Affiliated Hospital of Southwest Medical University
Song Su (13882778554@163.com)
The Affiliated Hospital of Southwest Medical University

Research Article

Keywords: SARS-CoV-2, COVID-19, Acute Pancreatitis, COVID syndrome

Posted Date: July 10th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3131112/v1

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at European Journal of Medical Research on August 16th, 2023. See the published version at https://doi.org/10.1186/s40001-023-01252-x.

Abstract

Introduction:

The existing literature on the combination of acute pancreatitis (AP) and COVID-19 is scarce. The objective of our study is to compare the clinical outcomes and occurrence of long COVID syndrome in AP patients with and without COVID-19, while investigating the potential impact of COVID-19 on the severity, mortality rate, and long COVID syndrome in these patients.

Materials and methods

This retrospective, observational study was conducted at a single center. It included patients aged 18 years and above who were diagnosed with AP during the pandemic. Patients were categorized into two groups based on the results of RT-qPCR testing: the COVID-19 positive group and the COVID-19 negative group. The study aimed to compare the severity of AP, mortality rate, and occurrence of long COVID syndrome between these two groups.

Result

A retrospective review was conducted on 122 patients diagnosed with acute pancreatitis between December 1, 2022, and January 31, 2023. Out of these patients, 100 were included in the study. The analysis revealed no significant differences in mortality rate, severity, and sequelae between AP patients with COVID-19 and those without COVID-19 ($p > 0.005$). However, a statistically significant difference was observed in the occurrence of long COVID syndrome, specifically in the presence of cough ($P = 0.04$).

Conclusion

This study demonstrates that the presence of COVID-19 in patients with pancreatitis does not lead to an increase in the mortality and severity rate of pancreatitis.

1. INTRODUCTION

Acute pancreatitis (AP) is a common gastrointestinal disease that typically requires hospitalization (1). Severe AP accompanied by organ failure is closely associated with poor patient prognosis and increased risk of mortality (2, 3). As of January 2023, there have been over 850 million reported cases of COVID-19 worldwide and over 6.6 million deaths (4). China adjusted its epidemic prevention policies on December 7, 2022, leading to a surge in cases from December 2022 to January 2023. During this period, the primary variant circulating in China was Omicron (5). Previous studies have shown a significantly increased risk of adverse outcomes and a mortality rate close to 20% in patients with concurrent AP and COVID-19 (6). However, with the increasing coverage of vaccines, the mortality rate of COVID-19 patients continues to

decline (7). The mortality rate of COVID-19 patients with AP may also undergo changes in the recent period.

Therefore, we conducted a retrospective review of all hospitalized patients with acute pancreatitis (AP) in our hospital, comparing the clinical outcomes and long-term COVID syndrome between patients with COVID-19-associated AP and those with COVID-19-negative AP.

2. Materials and Methods

2.1 Research Design

This is a single-center, retrospective, and observational study. We screened patients who visited the emergency department of our hospital from December 1, 2022, to January 31, 2023, using the hospital electronic system. The inclusion criteria were all patients with acute pancreatitis (AP) in the entire hospital, with available reverse transcriptase real-time (RT-qPCR) results, laboratory tests, and imaging results. If a patient had multiple admissions due to AP during the study period, only the last admission was considered for eligibility.

2.2 Research Definition

The diagnosis of acute pancreatitis (AP) is based on the revised Atlanta criteria (8). Comorbidities are classified using the Charlson Comorbidity Index (CCI) (9). The clinical diagnosis of COVID-19 is primarily based on epidemiological history, clinical manifestations, and laboratory testing methods. The laboratory testing method involves using an oropharyngeal swab sample for RT-qPCR (10). Based on the RT-qPCR test results, patients are categorized into positive and negative groups. Long COVID syndrome is defined as the presence of persistent symptoms and/or delayed or long-term complications lasting for more than 4 weeks after symptom onset (11). The severity of AP is determined using the Bedside Index for Severity in Acute Pancreatitis (BISAP) score (12). A BISAP score of ≥ 3 indicates severe AP, while a score of ≤ 2 indicates mild AP (13). We also utilize the Balthazar CT Severity Index (CTSI) to assess the severity of AP, with severity categorized as mild (0–3 points) or moderate to severe (4–10 points) (14).

Organ failure is defined as a Marshall score (15) of ≥ 2 in one or more of the three organ systems (respiratory, renal, and cardiovascular) initially described. The organ failure score is calculated based on the most extreme laboratory values or clinical measurements within the first 72 hours prior to hospital admission for all patients. The duration of organ failure is defined as transient ($\leq$ 48 hours) or persistent (> 48 hours).

2.3 Data Collection

Upon admission, clinical laboratory tests including white blood cell (WBC) count, lymphocyte (Lym) count, neutrophil (Neu) count, neutrophil-to-lymphocyte ratio (NLR), hematocrit (HCT), red cell distribution width (RDW), platelet (PLT) count, C-reactive protein (CRP), D-dimer levels, and imaging findings are recorded (Table 1). Patient history regarding alcohol consumption, family history (genetic diseases),

laboratory tests (hyperlipidemia), and diagnostic procedures such as computed tomography (CT), endoscopic ultrasound, magnetic resonance cholangiopancreatography (MRCP), and endoscopic retrograde cholangiopancreatography (ERCP) are examined to determine the etiology of the patient's condition. Patients in whom no cause is identified after evaluation are documented as having "unknown etiology".

Table 1
Comparison of laboratory parameters between positive and negative patients with COVID-19 on the first day of admission

Variables	Positive(n = 26,Mean ± SD)	Negative(n = 74,Mean ± SD)	P value
WBC ($\times10^9$/L)	10.95 ± 5.45	14.13 ± 7.26	**0.02**
NEU ($\times10^9$/L)	9.15 ± 5.67	12.09 ± 6.82	**0.03**
LYM ($\times10^9$/L)	1.4 ± 1.22	1.22 ± 0.8	0.48
MONO ($\times10^9$/L)	0.9 ± 1.99	0.76 ± 0.52	0.08
EOS ($\times10^9$/L)	0.04 ± 0.05	0.07 ± 0.11	0.23
BASO ($\times10^9$/L)	0.03 ± 0.04	1.25 ± 10.46	**0.037**
NEU-R (%)	78.72 ± 12.35	82.17 ± 11.94	0.14
LYM-R (%)	15.48 ± 12.78	10.21 ± 7.49	0.08
MONO-R (%)	5.52 ± 3.14	5.54 ± 3.7	0.54
EOS-R (%)	0.49 ± 0.72	0.64 ± 0.92	0.56
BASO-R (%)	0.23 ± 0.2	0.28 ± 0.39	0.40
RBC ($\times10^{12}$/L)	4.6 ± 0.93	4.44 ± 0.75	0.39
HGB (g/L)	139.35 ± 23.82	143.03 ± 29.22	0.57
HCT	0.4 ± 0.06	0.4 ± 0.07	0.90
PLT ($\times10^9$/L)	198.23 ± 74.73	217.92 ± 116.57	0.60
PT (s)	13.49 ± 1.58	13.36 ± 1.33	0.70
APTT (s)	30.13 ± 4.1	30.47 ± 6.49	0.49
TT (s)	17.32 ± 1.56	17.19 ± 2.14	0.40
ALT (U/L)	106.86 ± 197.63	78.89 ± 129.13	0.88
AST (U/L)	120.58 ± 274.38	92.71 ± 155.94	0.42

WBC: White Blood Cell,NEU: Neutrophil,LYM: Lymphocyte,MONO: Monocyte,EOS: Eosinophils,BASO: Basophils,NEU-R: Neutrophil rate,LYM-R: Lymphocyte rate,MONO-R: Monocyte rate,EOS-R: Eosinophil cell rate,BASO-R: Basophil cell rate,RBC: Red blood cell,HGB: Hemoglobin,HCT: Hematocrit,PLT: Platelet,PT: prothrombin time,APTT: Activated partial thrombin time,TT:Thrombin time,ALT: Alanine aminotransferase,AST: Aspartate aminotransferase,TBIL: Total bilirubin,TC: Total cholesterol,TG: Triglyceride,HDLC: High-density lipoprotein cholesterol,LDLC: Low-density lipoprotein cholesterol,Crea: Creatinine,GFR: Glomerular filtration rate,AMY: Amylase,PAMY: Pancreatic amylase,LPS: Lipase,NT-proBNP: N-terminal pro brain natriuretic peptide,PCT: Procalcitonin,IVGLU: Intravenous glucose,FBGLU: Fingertip blood glucose.

Variables	Positive(n = 26,Mean ± SD)	Negative(n = 74,Mean ± SD)	P value
TBIL (μmol/L)	21.89 ± 24.81	32.43 ± 58.49	0.33
TC (mmol/L)	6.84 ± 5.23	7.23 ± 5.07	0.28
TG (mmol/L)	6.63 ± 8.17	7.41 ± 7.7	0.32
HDLC (mmol/L)	1.3 ± 1.06	1.14 ± 0.7	0.47
LDLC (mmol/L)	2.78 ± 1.07	3.25 ± 1.45	0.18
Crea (μmol/L)	76.22 ± 46.92	73.5 ± 56.59	0.86
GFR (mL/min)	102.33 ± 33.25	103.62 ± 24.82	0.70
AMY (U/L)	608.53 ± 776.22	473.9 ± 682.32	0.60
PAMY (U/L)	510.77 ± 690.01	387.32 ± 579.75	0.65
LPS (U/L)	734.93 ± 880.1	706.84 ± 938.63	1.0
K (mmol/L)	3.96 ± 0.49	4.01 ± 0.64	0.90
Na (mmol/L)	138.77 ± 4.99	135.51 ± 6.33	**0.03**
Cl (mmol/L)	105.35 ± 6.34	103.46 ± 5.68	0.22
Ca (mmol/L)	2.33 ± 0.22	2.28 ± 0.25	0.41
NT-proBNP (ng/L)	557.1 ± 630.88	289.64 ± 462.1	0.06
PCT (ng/ml)	3.47 ± 9.53	1.38 ± 3.56	0.92
IVGLU (mmol/L)	9.2 ± 4.36	10.07 ± 6.35	0.70
FBGLU (mmol/L)	9.55 ± 3.66	11.02 ± 5.9	0.45

WBC: White Blood Cell,NEU: Neutrophil,LYM: Lymphocyte,MONO: Monocyte,EOS: Eosinophils,BASO: Basophils,NEU-R: Neutrophil rate,LYM-R: Lymphocyte rate,MONO-R: Monocyte rate,EOS-R: Eosinophil cell rate,BASO-R: Basophil cell rate,RBC: Red blood cell,HGB: Hemoglobin,HCT: Hematocrit,PLT: Platelet,PT: prothrombin time,APTT: Activated partial thrombin time,TT:Thrombin time,ALT: Alanine aminotransferase,AST: Aspartate aminotransferase,TBIL: Total bilirubin,TC: Total cholesterol,TG: Triglyceride,HDLC: High-density lipoprotein cholesterol,LDLC: Low-density lipoprotein cholesterol,Crea: Creatinine,GFR: Glomerular filtration rate,AMY: Amylase,PAMY: Pancreatic amylase,LPS: Lipase,NT-proBNP: N-terminal pro brain natriuretic peptide,PCT: Procalcitonin,IVGLU: Intravenous glucose,FBGLU: Fingertip blood glucose.

Patients who underwent interventional treatments (ERCP, PTC), surgical interventions (such as cholecystectomy), and pharmacological treatment for AP are documented. The length of hospital stay (intensive care/service), AP-related complications, and mortality rate are recorded. During the month of March 2023, a telephone follow-up was conducted for all patients to inquire about the presence of long COVID syndrome. Refusal to participate in the telephone follow-up or patient refusal to answer relevant questions is considered as loss to follow-up.

2.4 Statistical methods

The research data was evaluated using IBM SPSS Statistics version 27. The normality of quantitative data was analyzed using the one-sample Kolmogorov-Smirnov test, which helped determine whether to use parametric or non-parametric tests. Descriptive statistics were computed for frequency and percentage distributions, as well as for continuous variables, including mean, standard deviation, median, minimum, and maximum values. For comparing categorical variables between groups, the Pearson chi-square test and Fisher's exact test were employed. The Mann-Whitney U test was used to analyze differences between laboratory values and COVID-19 test results. Additionally, laboratory parameters were evaluated by comparing COVID-19 positive and negative patients with acute pancreatitis. A significance level of $P < 0.05$ was considered statistically significant.

3. Results

We conducted a retrospective analysis of 122 patients diagnosed with acute pancreatitis (AP) between December 1, 2022, and January 31, 2023. Among these patients, there were 100 individuals who met the inclusion criteria and had sufficient data recorded. The positivity rate for COVID-19 was found to be 26%. Among the included patients, 47.6% were male, with a mean age of 54.56 ± 16.90 years (n = 61), while 52.4% were female, with a mean age of 55.24 ± 19.00 years (n = 39).

The patients were divided into two groups: the COVID-19 positive group and the COVID-19 negative group. There were no significant differences in baseline characteristics between the two groups (Table 2). In terms of comorbidity distribution, there was no significant difference in the proportion of patients with a CCI score ≥ 5 between the positive and negative groups (Table 3). When comparing short-term organ failure between the two groups, there was no statistically significant difference ($P = 0.69$). Similarly, there was no statistically significant difference in the occurrence of persistent organ failure between the positive group (3.85%) and the negative group (4.05%) ($P = 1.0$). The BISAP score and Balthazar CT index also showed no statistically significant difference ($P = 0.88$, $P = 0.43$), indicating no significant difference in disease severity between the two groups. After analyzing the mortality rate among hospitalized patients, it was found that the mortality rate was 3.85% for the positive group and 4.05% for the negative group, with no statistically significant difference ($P = 1.0$).

Table 2
Demographic characteristics of patients

Variables	Category	Positive (n = 26)	Negative (n = 74)	P value
Age	n(mean ± SD)	46.46 ± 17.3	48.8 ± 12.8	0.53
Gender	Male / Female	15/11	46/28	0.69
BMI	mean ± SD	25.95 ± 3.54	25.49 ± 4.37	0.50
Smoke	n (%)	7 (26.92)	29 (39.19)	0.26
Alcohol	n (%)	8 (30.77)	26 (35.14)	0.69
Hypertension	n (%)	6 (23.08)	15 (20.27)	0.76
Diabetes	n (%)	8 (30.77)	24 (32.43)	0.88
Etiology	Hyperlipidemia, n (%)	7 (26.92)	21 (28.38)	0.97
	Gallstone, n (%)	8 (30.77)	21 (28.38)	
	Alcohol, n (%)	5 (19.23)	17 (22.97)	
	Others, n (%)	6 (23.08)	15 (20.27)	
Neocoronal vaccine	n (%)	19(95.0)*****	58(90.63)*****	1.0

BMI, body mass index (weight in kilograms divided by height in meters squared). A two-sided p value of less than 0.05 was considered statistically significant. (*) During hospitalization, there was no information about patient vaccination, so this information was obtained through follow-up. The percentage is the number of patients vaccinated compared to the total number of follow-up patients.

Table 3
COVID-19 positive-negative status and distribution of variables

Variables	Category	Positive (n = 26)	Negative (n = 74)	P value
CCI score	1–2, n (%)	24 (92.3)	69 (93.24)	1.0
	3–4, n (%)	1 (3.84)	3 (4.05)	
	≥ 5, n (%)	1 (3.84)	2 (2.7)	
BISAP score	< 3, n (%)	20 (76.92)	58 (78.38)	0.88
	≥ 3, n (%)	6 (23.08)	16 (21.62)	
Organ failure	None, n (%)	24 (92.3)	64 (86.49)	0.69
	Single-organ failure, n (%)	2 (7.69)	6 (8.11)	
	Double-organ failure, n (%)	0 (0)	3 (4.05)	
	Triple organ failure, n (%)	1 (3.84)	1 (1.35)	
Persistent organ failure, n (%)		1 (3.85)	3 (4.05)	1.0
Mortality, n (%)		1 (3.85)	3 (4.05)	1.0
Balthazar CT index	< 4, n (%)	15 (57.69)	36 (48.65)	0.43
	≥ 4, n (%)	11 (42.31)	38 (51.35)	
ICU	n (%)	2 (7.69)	3 (4.05)	0.83
Hospitalization length	mean ± SD	11.69 ± 8.79	9.75 ± 4.79	0.51

CCI: Charlson Comorbidity Index, BISAP score: Bedside index for severity in acute pancreatitis, ICU: Intensive care unit, COVID-19, the novel coronavirus disease 2019

A telephone follow-up was conducted for all AP patients (Table 4), and it was found that 16 individuals were lost to follow-up, resulting in a loss to follow-up rate of 16%. Regarding long COVID syndrome, only coughing showed a statistically significant difference (P = 0.04).

Table 4
Follow up table after 1 month faor positive and negative patients with COVID-19

Variables	Category	Positive(20)	Negative(64)	P value
Abdominal pain	n (%)	6(30.0)	8(12.50)	0.088
Recurrence*	n (%)	3(15.0)	3(4.69)	0.143
Poor appetite	n (%)	3(15.0)	8(12.50)	0.719
Nausea and vomiting	n (%)	3(15.0)	3(4.69)	0.143
Diarrhea	n (%)	2(10.0)	6(9.38)	1.0
Constipation	n (%)	1(5.0)	2(3.13)	0.563
Loss of weight	n (%)	3(15.0)	24(37.50)	0.098
Tired	n (%)	7(35.0)	17(26.56)	0.572
Cough	n (%)	3(15.0)	1(1.56)	**0.04**
Headache	n (%)	2(10.0)	1(1.56)	0.14
Dizziness	n (%)	2(10.0)	3(4.69)	0.588
Chest pain	n (%)	2(10.0)	1(1.56)	0.14
Myalgia	n (%)	1(5.0)	4(6.25)	0.659
Palpitate	n (%)	3(15.0)	4(6.25)	0.349
Dyspnea	n (%)	1(5.0)	0	0.238
Fever	n (%)	1(5.0)	0	0.238
Memory Loss	n (%)	1(5.0)	0	0.422
Anxiety	n (%)	3(15.0)	6(9.38)	0.439
Sleep disorder	n (%)	4(20.0)	8(12.50)	0.467
* It refers to the recurrence of pancreatitis within one month Sequelae				

Discussion

We present here the clinical and short-term outcomes of patients with acute pancreatitis (AP) admitted during the outbreak of the novel coronavirus pneumonia in China. We found that COVID-19 positive AP patients had similar mortality rates and disease severity compared to COVID-19 negative AP patients, with no statistically significant differences observed across various scoring systems. Follow-up at 1–2 months revealed that AP patients who tested positive for COVID-19 were more likely to experience cough symptoms (P = 0.04). Although there was a higher proportion of positive cases reporting abdominal pain, the difference was not statistically significant (P = 0.088).

A meta-analysis has indicated a high risk of adverse outcomes, with a mortality rate close to 20%, in patients with both AP and COVID-19 (6). However, in our study, we found no statistically significant difference in the mortality rates between AP patients with and without COVID-19 (P = 1.0). The mortality rate among AP patients with COVID-19 was 3.85%, which is considerably lower than the mortality rate reported in the literature.

The lower mortality rate observed in our study may be attributed to the fact that a majority of patients (91.7%) received vaccination. Research has shown that vaccines provide a significant level of protection against severe COVID-19, reducing hospitalization rates and mortality (7, 16). As of April 7, 2021, a total of 710 million vaccine doses have been administered globally, with at least one dose of an approved vaccine given to 5% of the world's population (17). The studies included in the article by Yang et al. (6) were published between 2020 and 2021, with most of the patients being admitted in 2020. Therefore, it can be inferred that the vaccine coverage among the patients included in Yang et al.'s article was extremely low, which could explain the lower mortality rate observed in our patients. Although there is evidence suggesting that SARS-CoV-2 can infect the pancreas and cause pancreatic injury (18), the BISAP score and Balthazar CT index indicated no difference in disease severity between the two groups. This may be due to the limited extent of pancreatic damage caused by the current strain of SARS-CoV-2, resulting in no statistically significant difference in disease severity and mortality rates between the two groups.

In our comparison of the initial laboratory test results between COVID-19 positive and negative patients on the day of admission, we found statistically significant differences ($P < 0.05$) in the counts of white blood cells, neutrophils, and eosinophils, while other results showed no statistically significant differences ($P > 0.05$). These differences may be attributed to the viral infection.

After a short-term follow-up of one month post-discharge, we found that the most commonly reported symptoms of long COVID syndrome among COVID-19 positive patients were fatigue (35%) followed by abdominal pain (30%). Although both symptoms were relatively high in proportion compared to COVID-19 negative patients, there was no statistically significant difference ($P > 0.05$). The only symptom that showed a statistically significant difference was cough ($P = 0.04$). The prevalence of cough in our COVID-19 patients after discharge (15%) was similar to what has been reported in other studies (19). Research has shown that vaccinated individuals and those infected with the Omicron variant have a lower risk of developing long COVID syndrome (20). This may explain why there was no difference in long COVID syndrome among our patients.

Additionally, studies have reported that even post-infection vaccination can alleviate long COVID syndrome (21). Therefore, it is recommended that patients who have not received the vaccine after infection should consider getting vaccinated to mitigate the symptoms of long COVID syndrome.

Limitations of the study

As this study is retrospective, there may be selection bias, and the results may not fully reflect the overall outcomes of patients with COVID-19-associated pancreatitis. Our follow-up was conducted via telephone, which introduces the possibility of recall bias. Additionally, a small proportion of patients were lost to follow-up, which could potentially impact the results. The sample size of our study was relatively small, with only 100 patients. This study was conducted at a single center, which may limit the generalizability of the results. The follow-up period was relatively short (1–2 months), and longer-term follow-up was not conducted. Long COVID-19 syndrome typically lasts for 4–8 weeks or longer. Therefore, it is possible that some patients who tested negative for COVID-19 upon admission may have been infected prior to admission or after discharge, which could introduce bias in the follow-up results of long COVID-19 syndrome.

Conclusions

Our research findings indicate that there is no significant difference in clinical outcomes and short-term prognosis between patients with COVID-19-related pancreatitis and those without COVID-19 infection. Furthermore, we observed that individuals who have been vaccinated against COVID-19 and subsequently contract COVID-19-related pancreatitis generally do not require additional medical care.

Declarations

Author contribution(s)

Data collection and organization were carried out by Zhang Jinchang and Kang Maoji. Zhang Jinchang and Luo De performed the statistical analysis and completed the writing of this manuscript. Li Bo provided valuable suggestions for the manuscript's revisions, while Su Song was responsible for the editing and final review of the manuscript. All authors rigorously assessed the research design, contributed to manuscript editing, and read and approved the final version.

Funding

This study was supported by the National Natural Science Foundation of China (No. U22A2039).

Availability of data and materials

The datasets utilized and/or analyzed during the present study are accessible from the corresponding author upon reasonable request.

Ethics approval and consent to participate

This retrospective and observational study did not provide any additional interventions to the included patients. The retrospective study design has been approved by the Clinical Trial Ethics Committee of the Affiliated Hospital of Southwest Medical University, China (Approval No: KY2023190).

This study was conducted in accordance with the Helsinki Declaration. A written informed consent form has been exempted by the ethics review committee because we only retrospectively extracted anonymous data without any protected information. Each patient participating in this study was assigned a unique identifier, and all anonymous patient data were recorded and analyzed in relation to this identifier.

Consent for publication

The research findings presented in this work have not been previously published, and the publication of this manuscript has received approval from all co-authors.

Competing interests

The authors declare that there is no conflict of interest.

References

1. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, et al. Acute pancreatitis. Lancet. 2020;396(10252):726-34.
2. Schepers NJ, Bakker OJ, Besselink MG, Ahmed Ali U, Bollen TL, Gooszen HG, et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. Gut. 2019;68(6):1044-51.
3. He W, Chen P, Lei Y, Xia L, Liu P, Zhu Y, et al. Randomized controlled trial: neostigmine for intra-abdominal hypertension in acute pancreatitis. Crit Care. 2022;26(1):52.
4. Hromić-Jahjefendić A, Barh D, Uversky V, Aljabali AA, Tambuwala MM, Alzahrani KJ, et al. Can COVID-19 Vaccines Induce Premature Non-Communicable Diseases: Where Are We Heading to? Vaccines (Basel). 2023;11(2).
5. Ma E, Ai J, Zhang Y, Zheng J, Gao X, Xu J, et al. Omicron infections profile and vaccination status among 1881 liver transplant recipients: a multi-centre retrospective cohort. Emerg Microbes Infect. 2022;11(1):2636-44.
6. Yang F, Huang Y, Li T, Fu Y, Sun C, Xu Y, et al. Prevalence and outcomes of acute pancreatitis in COVID-19: a meta-analysis. Gut. 2022;71(7):1451-3.
7. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis. 2022;22(9):1293-302.
8. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-11.
9. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.
10. Rai P, Kumar BK, Deekshit VK, Karunasagar I, Karunasagar I. Detection technologies and recent developments in the diagnosis of COVID-19 infection. Appl Microbiol Biotechnol. 2021;105(2):441-

55.

11. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. Nat Med. 2021;27(4):601-15.
12. Wu BU, Johannes RS, Sun X, Tabak Y, Conwell DL, Banks PA. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut. 2008;57(12):1698-703.
13. Singh VK, Wu BU, Bollen TL, Repas K, Maurer R, Johannes RS, et al. A prospective evaluation of the bedside index for severity in acute pancreatitis score in assessing mortality and intermediate markers of severity in acute pancreatitis. Am J Gastroenterol. 2009;104(4):966-71.
14. Cheng T, Han TY, Liu BF, Pan P, Lai Q, Yu H, et al. Use of Modified Balthazar Grades for the Early Prediction of Acute Pancreatitis Severity in the Emergency Department. Int J Gen Med. 2022;15:1111-9.
15. Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med. 1995;23(10):1638-52.
16. Lai FTT, Yan VKC, Ye X, Ma T, Qin X, Chui CSL, et al. Booster vaccination with inactivated whole-virus or mRNA vaccines and COVID-19-related deaths among people with multimorbidity: a cohort study. Cmaj. 2023;195(4):E143-e52.
17. Mathieu E, Ritchie H, Ortiz-Ospina E, Roser M, Hasell J, Appel C, et al. A global database of COVID-19 vaccinations. Nat Hum Behav. 2021;5(7):947-53.
18. Zheng L, Zhang L, Zheng Y, An J, Wen G, Jin H, et al. Digestive system infection by SARS-CoV-2: Entry mechanism, clinical symptoms and expression of major receptors (Review). Int J Mol Med. 2023;51(3).
19. Carfì A, Bernabei R, Landi F. Persistent Symptoms in Patients After Acute COVID-19. Jama. 2020;324(6):603-5.
20. Howe S, Szanyi J, Blakely T. The health impact of long COVID during the 2021-2022 Omicron wave in Australia: a quantitative burden of disease study. Int J Epidemiol. 2023;52(3):677-89.
21. Richard SA, Pollett SD, Fries AC, Berjohn CM, Maves RC, Lalani T, et al. Persistent COVID-19 Symptoms at 6 Months After Onset and the Role of Vaccination Before or After SARS-CoV-2 Infection. JAMA Netw Open. 2023;6(1):e2251360.