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Author Contribution

All authors drafted the manuscript. FW revised the final manuscript. FW, JF and YZ were responsible for summarizing all data related to this study.

Conflict of interests

None declared.

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Introduction

Since December 2019, novel coronavirus (SARS-CoV-2)-infected pneumonia (COVID-19) occurred in Wuhan, and rapidly spread throughout China.¹ Recent studies mainly focused on the epidemiological and clinical characteristics of patients with confirmed infection.¹⁻³ Little attention has been paid to the pancreatic injury caused by SARS-CoV-2 infection.

Methods

Fifty-two patients with COVID-19 pneumonia were admitted to Zhongnan Hospital of Wuhan University from January 20th to February 28th, 2020. The disease was confirmed by detecting SARS-CoV-2 nucleic acid in throat swab samples using the RT-PCR assay method. On admission, all patients had a comprehensive laboratory examination, including blood cytology, biochemistry and inflammatory indicators. Pancreatic injury was defined as any abnormality in amylase (normal range: 0~90 U/L) or lipase (0~70 U/L). Serious illness was defined if satisfying at least one of the following items: (i) breathing rate ≥ 30 /min; (ii) pulse oximeter oxygen saturation (SpO₂) $\leq 93\%$ at rest; (iii) ration of partial pressure of arterial oxygen (PaO₂) to fraction of inspired oxygen (FiO₂) ≤ 300 mmHg (1mmHg=0.133kPa). During the hospitalization, each patient had a swab virus test every other day. Negative conversion time of SARS-CoV-2 was defined as the interval between symptom onset and the first of two consecutive negative virus tests.

Categorical data were described as percentages, and continuous data as mean with standard error (SD). Pearson correlation analysis was used to compare variables between the COVID-19 patients with and without pancreatic injury. A two-sided $P < 0.05$ was considered statistically significant.

Results

Among the 52 patients with COVID-19 pneumonia, the incidence was 33% for heart injury (abnormal LDH or creatine kinase), 29% for liver injury (any abnormality in AST, ALT, GGT or ALP), 17% for pancreatic injury, 8% for renal injury (abnormal creatinine), and 2% for diarrhea. The nine patients with pancreatic injury had an average age of 55 years

ranging from 25 to 71 (**Table 1**). Five patients had underlying diseases such as hypertension, diabetes and heart disease. The most common chief complaints were fever and respiratory symptoms. Four patients were categorized into serious illness on admission. In laboratory tests, these patients were characterized by a decrease in lymphocytes and the subsets, and an increase in hepatic and myocardial enzymes and inflammatory indicators. Seven patients received corticosteroid therapy, and one with mechanical ventilation. The median time of SARS-CoV-2 negative conversion was 22 days from symptom onset.

Compared with the patients without pancreatic injury, those with pancreatic injury had a higher incidence of anorexia and diarrhea, severer illness on admission, lower level of CD3⁺ T-cell and CD4⁺ T-cell, higher level of AST, GGT, creatinine, LDH and ESR. Two groups showed no significant difference in corticosteroid treatment, mechanical ventilation or virus negative conversion time.

Discussion

In this study, we found that the incidence of pancreatic injury was not very low in the patients with COVID-19 pneumonia. In the previous SARS-CoV infected pneumonia (2003), the virus was detected not only in the tissues of lung, liver, kidney and intestine but also in pancreas, indicating pancreas as potential coronaviral targets.⁴ Moreover, the SARS-CoV receptor of ACE2 was highly expressed in pancreas islets, and SARS-CoV infection caused the damage of islets and subsequent acute diabetes.⁵ In our study of nine COVID-19 patients with pancreatic injury, six patients were found abnormal in blood glucose. These findings suggested the pancreatic injury in COVID-19 might be caused directly by the cytopathic effect mediated by local SARS-CoV-2 replication. On the other hand, the pancreatic injury might be caused indirectly by systemic responses to respiratory failure or the harmful immune response induced by SARS-CoV-2 infection, which also led to the damage in multiple organs. In this study, heart, liver and renal injuries were detected simultaneously. Third, most patients took antipyretics before admission, which could also cause drug-related pancreatic injury.

In conclusion, these results demonstrate potential mild pancreatic injury patterns in patients with COVID-19 pneumonia, and these may be related to direct viral involvement of the pancreas or from secondary enzyme abnormalities in the context of severe illness without substantial pancreatic injury. They do not demonstrate clinically severe pancreatitis as a common manifestation. Further research and larger series are warranted to evaluate whether a subset of patients have clinical pancreatitis as a presenting or concomitant disease entity.

References

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Table 1. Characteristics of COVID-19 pneumonia patients with pancreatic injury.

Variable, No (%) or Mean \pm SD	COVID-19 with pancreatic injury (PI)										Without PI	P value
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Overall	N=43	
Age (y)	25	55	62	65	66	71	36	56	62	55 \pm 15	52 \pm 18	0.633
Male	Y	Y	Y	Y	Y	Y	N	N	N	6 (67)	18 (42)	0.181
Comorbidities												
Hypertension	N	Y	Y	N	Y	N	N	N	N	3 (33)	7 (16)	0.246
Diabetes	Y	N	Y	N	Y	N	N	N	N	3 (33)	7 (16)	0.246
Heart	N	N	N	N	N	N	N	N	Y	1 (11)	2 (5)	0.460
Cerebrovascular	N	N	N	N	N	N	N	N	N	0 (0)	2 (5)	0.519
Respiratory	N	N	N	N	N	N	N	N	N	0 (0)	1 (2)	0.652
Chief complaints on admission												
Fever	Y	Y	Y	Y	Y	Y	Y	Y	N	8 (89)	26 (60)	0.107
Chest distress/breath shortness	Y	N	Y	Y	Y	N	N	N	N	4 (44)	7 (16)	0.062
Cough	N	N	N	N	Y	Y	N	N	Y	3 (33)	10 (23)	0.535
Fatigue	N	N	N	Y	N	N	N	N	N	1 (11)	9 (21)	0.506
Anorexia	N	N	N	N	N	N	N	Y	N	1 (11)	0 (0)	0.027
Diarrhea	N	N	N	Y	N	N	N	N	N	1 (11)	0 (0)	0.027
Headache	N	N	N	N	N	N	N	N	N	0 (0)	1 (2)	0.652
Severe illness on admission	Y	N	Y	Y	Y	N	N	N	N	4 (44)	6 (14)	0.035
Blood cytology												
Leukocytes (3.5~9.5 $\times 10^9$ /L)	5.31	6.29	4.86	8.03	10.7	4.94	4.11	8.54	2.77	6.17 \pm 2.48	5.21 \pm 3.33	0.421
Neutrophils (1.8~6.3 $\times 10^9$ /L)	4.34	4.61	3.86	7.24	10.16	3.81	3.41	6.82	1.58	5.09 \pm 2.56	3.76 \pm 3.38	0.276
Monocytes (0.1~0.6 $\times 10^9$ /L)	0.34	0.79	0.28	0.38	0.25	0.37	0.10	0.76	0.26	0.39 \pm 0.23	0.41 \pm 0.17	0.841
Platelets (125~350 $\times 10^9$ /L)	219	248	112	279	179	74	209	220	134	186 \pm 67	198 \pm 87	0.701
Lymphocytes (1.1~3.2 $\times 10^9$ /L)	0.62	0.87	0.71	0.38	0.29	0.76	0.59	0.95	0.90	0.67 \pm 0.23	0.94 \pm 0.49	0.119
CD3+ T-cell (805~4459/ μ L)	300	-	292	-	184	562	362	129	542	339 \pm 165	948 \pm 686	0.027
CD4+ T-cell (345~2350/ μ L)	108	-	114	-	86	304	103	81	236	147 \pm 87	503 \pm 367	0.016
CD8+ T-cell (345~2350/ μ L)	189	-	170	-	96	239	223	45	277	177 \pm 82	397 \pm 380	0.138

CD4/CD8 ratio (0.96~2.05)	0.57	-	0.67	-	0.90	1.27	0.46	1.78	0.85	0.93 ± 0.46	1.68 ± 1.07	0.078
CD19+ B-cell (240~1317/μL)	154	-	79	-	146	38	88	49	51	86 ± 47	147 ± 85	0.078
CD16+CD56+ NK-cell (210~1514/μL)	322	-	609	-	136	142	240	8	12	210 ± 209	210 ± 148	0.994
Blood biochemistry												
ALT (9~50 U/L)	175	54	47	48	55	13	13	11	23	49 ± 51	30 ± 32	0.167
AST (15~40 U/L)	90	69	82	55	71	29	19	16	33	52 ± 28	29 ± 15	0.001
ALB (40~55 g/L)	43.9	37	38.9	36.6	34.4	36.1	43	29.4	32.5	36.9 ± 4.6	36.7 ± 5.0	0.943
GLB (20~30 g/L)	32.1	35.3	37.6	36.3	28.8	29.0	29.7	27.3	28.7	31.6 ± 3.8	30.0 ± 6.9	0.499
GGT (8~57 U/L)	154	63	75	123	51	54	13	13	20	63 ± 49	31 ± 19	0.003
ALP (30~120 U/L)	74	84	76	106	85	52	63	87	65	77 ± 16	74 ± 30	0.794
Creatinine (64~104 μmol/L)	89.3	130.9	158.7	106.4	73.7	68.9	59.0	109.2	57.8	94.9 ± 34.5	61.6 ± 17.6	0.000
Glucose (3.9~6.1 mmol/L)	15.26	6.90	9.49	8.42	13.78	5.44	8.85	4.91	5.63	8.74 ± 3.66	11.11 ± 24.81	0.779
LDH (125~243 U/L)	292	435	646	94	533	186	207	192	281	318 ± 182	219 ± 81	0.019
Creatinine kinase (<171 U/L)	472	297	253	654	195	191	69	20	125	253 ± 201	120 ± 206	0.093
D-dimer (0~500 ng/mL)	233	261	410	382	633	395	147	-	251	339 ± 150	889 ± 1757	0.385
Amylase (0~90 U/L)	84	107	113	109	149	136	100	151	86	115 ± 25	52 ± 18	0.000
Lipase (0~70 U/L)	83	47	45	112	124	21	45	85	77	71 ± 34	31 ± 13	0.000
Blood inflammatory indicators												
CRP (0~10 mg/L)	10.0	98.0	137.3	161.1	104.5	11.4	20.0	2.3	15.0	62.2 ± 62.6	35.5 ± 47.0	0.162
ESR (0~15 mm/h)	8	93	56	82	62	-	34	-	19	51 ± 32	25 ± 23	0.016
IL-6 (0.1~2.9 pg/mL)	18.89	-	21.44	-	19.90	54.68	2.54	7.06	35.03	22.79 ± 17.56	19.76 ± 24.07	0.756
Hospitalized treatment												
Corticosteroid	Y	N	Y	Y	Y	Y	Y	Y	N	7 (78)	18 (42)	0.051
Mechanical ventilation	N	N	N	Y	N	N	N	N	N	1 (11)	3 (7)	0.679
Virus negative conversion time (days)*	40	20	13	17	21	25	19	21	18	22 ± 8	17 ± 8	0.090

COVID-19, coronavirus disease 2019; PI, pancreatic injury; No, number; SD, standard error; IL, interleukin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; GLB, globulin; GGT, glutamyltranspetidase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; Y, yes; N, no.

*, the interval between symptom onset and the first of two consecutive negative virus tests.