International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 20-07-2020; Accepted: 05-08-2020; Published: 21-08-2020
www.medicalsciencejournal.com
Volume 6; Issue 8; 2020; Page No. 210-214

Acute pancreatitis and its impact in COVID-19 pandemic: A prospective study

Sathik[1], Balraj[2], Deepan Karthick[3], Rajmohan[4], JA Jayalal[5]
[1, 3, 4] Assistant Professors Department of Surgery Tirunelveli Medical College, Tamil Nadu, India
[2] Postgraduate resident, Department of Surgery Tirunelveli Medical College, Tamil Nadu, India
[5] Professor of Surgery, Tirunelveli Medical College and, Tamil Nadu, India

Abstract
Coronavirus disease 2019 (COVID-19) caused by the novel SARS-COV-2 typically presents with pulmonary symptoms and complications. However various extrapulmonary manifestations and resultant complications are studied and reported. Extra-pulmonary symptomatology of COVID-19 has drawn significant attention. One among this in the Gastroenterology is Pancreatitis but it is rare. However, the general incidence of Pancreatitis have shown a upward trend in the pandemic with increased amount of use of alcohol adulterated and spurious it is mandatory to check for all cases presenting with signs and symptoms of acute pancreatitis with COVID testing and aggressive conservative management.
Material and Methods: It is a prospective study enrolling all the first 50 patients presented with symptoms of acute pancreatitis from April 2020 to July 2020 in the department of surgery Tirunelveli medical college hospital. Cases were studied with reference to clinical/biochemical/radiological signs of pancreatitis. Treatment was planned according to the severity of pancreatitis and presence or absence of complications with either conservative or surgical methods. All patients were taken RT-PCR swab testing to confirm the presence or absence of the SARS-COV -2 infections. Patients were followed up for 1 month to look for recurrence or complications developing after discharge.
Results: 82% patients were male and 18 % female. The highest incidence was noted in 30-50 years age group (mean – 43.5 years, Median 44 yrs., Standard deviation 11.342). More common among unskilled workers. Alcohol was the most common cause (58% patients). Abdominal pain is the most common mode of presentation (90%), and epigastric tenderness is most common sign (90%). All the patients except one were managed conservatively. Three patients (6%) tested positive for COVID -19 and they had conservative management. 30% cases had moderate,12% had severe and 58% cases had mild pancreatitis.
Comorbidity was present with Hypertension in 32%, Diabetes 22% and 36% presented without any comorbidity. Morality was 2% in our study.
Conclusions: The accurate diagnosis and aggressive management of acute pancreatitis in COVID-19 patients are mandatory to prevent the double-blind impact on the target organs. All cases of acute pancreatitis shall be evaluated for COVID-19 infection also to plan for treatment protocol and surgeons should adhere to safety protocols. The possible association between COVID-19 and pancreas at some point of time during its course, should be kept in mind and diagnosis shall not depend upon isolated raise of pancreatic enzyme.

Keywords: pancreatitis, Covid-19, ARDS, Atlanta score

Introduction
The pancreas is an endocrine organ with vide endo and exocrine function responsible for metabolism and digestion. Pancreas produces many important hormones including insulin, glucagon, somatostatin, and pancreatic polypeptide which circulate in the blood. Pancreas as a digestive organ secrete pancreatic juice containing digestive enzymes that assist digestion and absorption of nutrients in the small intestine. These enzymes help the further breakdown of carbohydrates, proteins, and lipids in the chyme.
Though Pancreatitis has been recognized since antiquity, but the importance of pancreas and the severity of its inflammatory disorders were realized only in the middle of 19th century. More than a century after its comprehensive description, acute pancreatitis (AP) remains a common disorder with devastating consequences. Pancreatitis by itself is a disease which is unique, protean and extrudes into the diagnostic arena.
Although most episodes are mild and self-limiting, up to a fifth of patients will develop a severe attack that can be fatal. The presentation of wide spectrum of symptoms gives the clinician a heartbreaking exercise to bring back the patient from the clutches of the disease process. Pancreatitis is inflammation of the pancreatic parenchyma. For clinical purpose it is useful to divide pancreatitis into acute, which present as an emergency and chronic, which is prolonged and frequently lifelong disorder resulting from development of fibrosis within the pancreas. Acute pancreatitis is a wide spectrum disease ranging from mild self-limiting symptoms to fulminant processes with multiorgan failure and high mortality.
Acute pancreatitis is a common condition involving the pancreas and present commonly with Upper abdominal pain that radiates to back, feels worse after eating, fever, rapid pulse, nausea, vomiting and tenderness in the epigastrium. Gallstones and alcoholism together account for 80% of Acute pancreatitis. It is noted due to urbanisation, increase in stress level, increase use of alcohole and an improved ability to diagnose the disease results in an increase incidence of disease in past 3 decades. Acute pancreatitis has been a cause of significant morbidity and mortality.
Chronic pancreatitis (CP) is a chronic pancreas exocrine

part inflammation which is accompanied by parenchymal destruction and fibrosis. Alcohol consumption and smoking are the most common risk factors. It can present as episodes of acute inflammation in a previously injured pancreas or as chronic damage with persistent pain or malabsorption.

Diagnoses is often by the clinical symptoms and supported by the estimation of serum amylase. In addition, estimation of serum lipase, trypsinogen, or iso amylase assay is confirmatory and will increase the diagnostic yield. Diagnostic radiological procedures such as sonography, computed tomography, and MRI are often helping to quantify and grade the disease. CECT remains the gold standard modality of choice where areas of hypoperfusion correlate with necrosis. The revised Atlanta classification is used to make the correct diagnosis with at least two of the following three criteria:

1. typical abdominal pain,
2. serum amylase or lipase > 3 times the upper normal limit,
3. characteristic findings on diagnostic imaging;

Improper and inadequate assessment the severity of the disease often results in an increased mortality. Various prognostic scoring systems have been developed involving multiple factor. The mortality rate for mild cases is around 1% but for those who have developed severe systemic inflammatory response and multi-organ failure (5-10% cases) the mortality rate varies from 20-50

The data is available in literature regarding the incidence and management of pancreatitis in this pandemic COVID era are scarce and evolving. Coronavirus disease 2019 (COVID-19) though typically presents with pulmonary symptoms studies shows they also present with Extra-pulmonary symptomatology.

Meta-analysis review of 47 studies comprising 10,890 COVID-19 patients showed that in less than 10% of cases, gastrointestinal symptoms are present with a pooled prevalence of 7.8% for nausea/vomiting, 7.7% for diarrhoea and 2.7% for abdominal pain and 15% for liver enzyme abnormalities (transaminitis) [1]. Surgeons involved in the management of Acute pancreatitis must be cautious of its existence in the context of COVID-19 as with the increasing prevalence of COVID-19 it is expected that we would encounter more of its atypical presentations.

Objectives of the study were to study the demographic characteristics of pancreatitis, and to study the various associated comorbid conditions in acute pancreatitis, the clinical presentation of pancreatitis and its management in the COVID pandemic and impact of the SARS-Cov-2 infection in Pancreatitis

Aim

The purpose of this study is to analyze incidence and manifestations of pancreatitis in this COVID era and the impacts of SARS-COV-2 infection on pancreatitis.

Methodology

This is prospective analytical cohort study in a series of patients who underwent treatment for pancreatitis between April 2020 to July 2020 in the department of general surgery, Tirunelveli medical college and hospital. 50 cases were studied in the period and its outcome was monitored and studied with demographic pattern, comorbidities and SARS-COV-2 infections.

Statistical analysis was performed using SPSS 20. Univariate analysis results are calculated with a mean and SD or percentage. Statistical significance was considered when $P < .05$.

Results

Demographic data

In our study involving 50 patients 41 (82%) 9 (18%) were female**.** The highest incidence was noted in 30-50 years age group. The mean age of involvement were 43.5 year and the Median was 44 yrs., Standard deviation 11. 342.The data are tabulated in Figure 1 and 2.

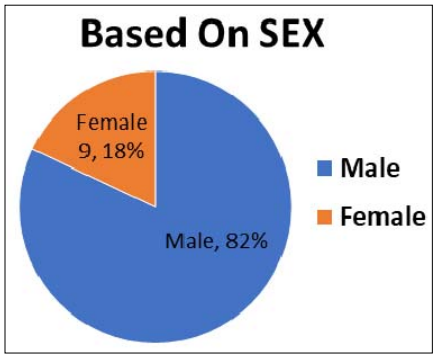

Fig 1: sex distribution of the patients

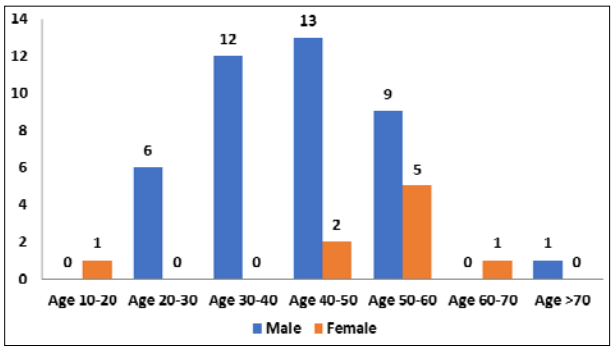

Fig 2: Age and sex distribution

RT PCR Positive for COVID -19 in Patients with Appendicitis

The patients diagnosed to have appendicitis based on clinical, biochemical and radiology were subjected to swab testing for RTPCR and three patients were found to be positive depicted in Figure 3.

Total number of patients: 50 (100%)

RTPCR Positive: 03 (6 %)

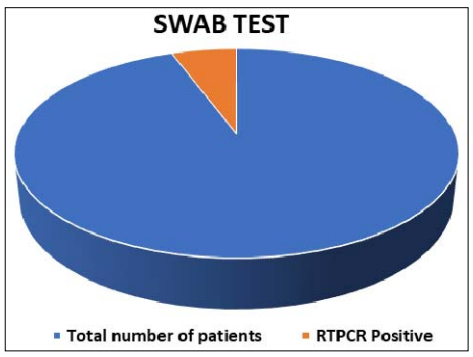

Fig 3: RTPCR test results for the patients with acute pancreatitis.

Associated Comorbiditis

The patients were assessed to note the presence of other associated comorbid conditions like Diabetes, Hypertension, CAD, Obesity, high risk behaviour, chronic liver and kidney disorders. The patients had statically significant comorbidities p= >. 004.Combination of diseases like both Diabetes and Hypertension were noted. The data are tabulated in Table 1 and Figure 4.

Table 1: Pancreatitis with comorbidities

NO	Comorbidities	Number of patients	Percentage	Chi-square	P value
	Diabetes	15	30	3.6462	.0500
	Hypertension	3	6	28.2435	< 0.00001
	Diabetes with Hypertension	8	16	16.2481	< 0.00005
	Heart Disease	3	6	28.2435	< 0.00001
	Chronic Renal disease	6	12	20.5737	< 0.00001
	Chronic liver disease	12	24	9.2925.	.002301
	Gall stones	3	6	28.2435	< 0.00001
	Obesity	24	48	0.0533	.817345
	Alcoholism	40	80	12.5	.000407

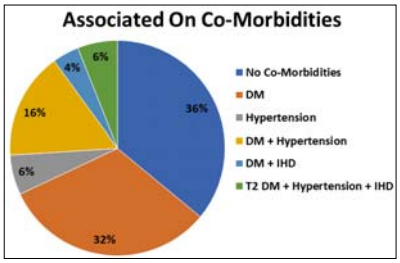

Fig 4: Pancreatitis with comorbidities

The severity of the cases were assessed using the Ranson score both at admission and after 48 hours and the values are shown in Figure 5 and patients were assigned to have mild, moderate and severe pancreatitis and shown in Figure 6

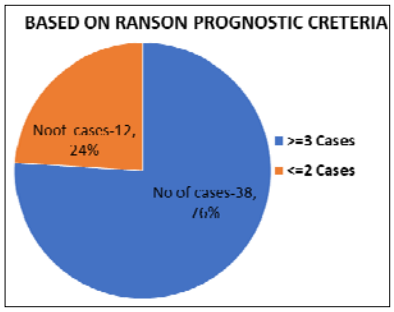

Fig 5: Assessment of severity based on RANSON score

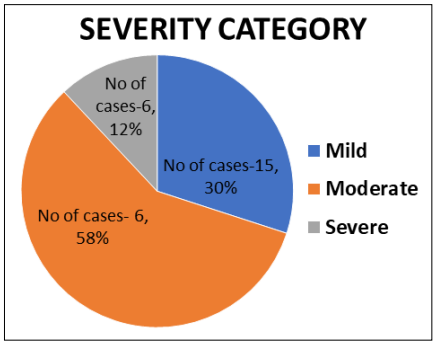

Fig 6: Grade of severity of cases

All the non COVID -19 patients were treated conservatively in the surgical ward and one patient developed splenic vein thrombosis with Perforation of the stomach and treated with emergency laparotomy and correction. The three patients who tested positive for COVID-19 are treated in the designated ward conservatively. Except for the cases in which intervention is done all cases recovered and discharged. The duration hospital varied from in average 5-15 days and shown in Figure 7.

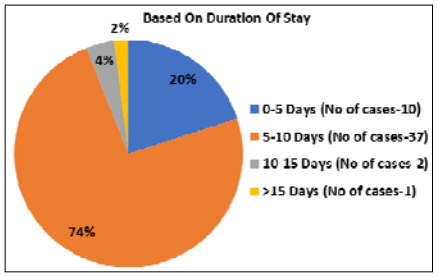

Fig 7: Duration of hospital stay.

Discussion

Clinical Spectrum of Pancreatic Injury in COVID-19

ACE2 expression along the GI tract suggests the digestive system as a potential route for COVID-19, Zhang *et al* recently described [1]. ACE2 is also noted to be expressed in the pancreas [2] and significant lipase elevations, suggestive of pancreatic involvement, have been reported among patients with COVID-19 [3]. However, the clinical implications of these findings with regards to COVID-19 susceptibility among patients with prior pancreatitis are unclear.

As per the clinical reports available, there can be

- an isolated rise in the pancreatic enzymes without any clinical or radiological evidence of Acute pancreatitis,
- subclinical disease with only serological and/or radiological evidence of Acute pancreatitis
- "pancreatitis-like clinical presentation",
- an overt episode of Acute pancreatitis.

John Gubatan *et al*. reported the prevalence of COVID-19 among patients with prior pancreatitis was 7.8% (8/102). Bendavid E etal in his series reported the prevalence of COVID-19 among patients with prior pancreatitis is 7.8% which is greater than the population-weighted prevalence of SARS-CoV-2 positive serology in our background population at 2.8% in the santa clara country [5].

Few reported cases of COVID with acute pancreatitis in this pandemic are tabulated in Table 2.

Table 2: Reported cases of acute pancreatitis in COVID -19 patients

Author	Age/sex	Gastrointestinal symptoms/signs	Other symptoms	Lab parameters		Abdominal imaging	Severity grading	Organ failure
				Serum amylase Serum lipase	CRP			
Aloysius *et al*. [6]	36 F	Nausea, vomiting, diarrhoea, severe epigastrium pain and tenderness	Fever, dry cough, progressive dyspnoea	325 U/L 627 U/L	19.5 mg/L	CT scan: unremarkable pancreas and gallbladder	Severe (Modified Atlanta)	Respiratory
Hadi *et al*. [7]	47 F	None	Fever, headache, neck pain, anorexia, sore throat, dyspnoea	>1500 U/L NA	>200 mg/L	Abdominal ultrasound: diffusely voluminous pancreas without focal lesions or gallstones	Severe (Glasgow score 5)	Respiratory Renal
Anand *et al*. [8]	59 F	Abdominal pain, constipation	Fever	NA NA	62.7 g/L	CT scan: diffuse edematous pancreatitis	NA	NA

Elevated Pancreatic enzymes vs Acute pancreatitis

Wang *et al*. earlier reported 17% incidence of pancreatic injury among 52 patients with COVID-19 pneumonia **(10)**. However as per the accepted International criteria **(13)** that acute pancreatitis is defined as acute pain abdomen associated with a 5-fold increase in serum pancreatic enzymes, and imaging showing acute alterations of the pancreatic gland none of their patients had an episode of acute pancreatitis. However, there was increase in serum pancreatic enzymes, such as amylase (24.5% of the cases) and lipase (16.4% of the cases), and only one had a three-fold increase in this enzyme without pain and alteration of the pancreatic gland at imaging. This elevation of the serum pancreatic enzymes were not related to either the presence of symptomatic diarrhea or nausea/vomiting, or to the IgM and IgG status.

Hadi *et al*. reported two of three family members with COVID-19 had acute pancreatitis **(7)**. However, the diagnosis is made based on the history of pain abdomen and elevated enzymes, but no significant radiological evidence was reported. Anand *et al*. reported a case of COVID-19 who initially presented with fever, cough, sore throat and myalgia but developed abdominal symptoms 5 days after the discharge. CT scan showed diffusely edematous pancreatitis [8]. None of the cases reported so far in the literature had necrotising pancreatitis even though some were classified as severe, and none required any intervention for pancreatitis-related local complications.

In the study reported in 67 severe COVID-19 by Liu *et al*. there was 17% incidence of pancreatic injury in cases although injury was evident on computed tomography (CT) scan in only 7.46% cases, mainly as focal pancreatic enlargement or pancreatic ductal dilatation [12]. In mild pancreatitis the incidence of pancreatic injury was low (1.85%) [12].

In our study out of 50 cases presented with mild to severe pancreatitis three patients were tested positive for SARS-COV-2 virus and all had only come mild pancreatitis with RANSOM Score less than 2. In our study There was no statiscally significant difference with regards to obesity, smoking status, alcohol use, diabetes mellitus, ACE inhibitor or angiotensin receptor blocker use between patients with or without COVID-19.

Mechanisms of Pancreatic Injury in COVID-19

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) seems to have an affinity for the pancreas as Angiotensin-converting enzyme 2 (ACE2) receptor is expressed in both in the exocrine glands and islet cells of Pancreas [2, 12] and it is relatively higher in the pancreas than in the lungs. Due to the direct cytopathic effect of SARS-CoV-2 mediated by its local replication it can cause substantial injury to the pancreatic cells. SARS-CoV-2 by its dysregulated immune response induced by that targets pancreas in addition to the lungs and kidneys can induce acute pancreatitis and organ failure [10] in a patient with COVID-19 who might otherwise be asymptomatic or mildly symptomatic. Drug-induced injury either directly (e.g. use of nonsteroidal anti-inflammatory drugs (NSAID) or glucocorticoids) or indirectly (through tocilizumab-induced hypertriglyceridemia) [14] can result in acute pancreatitis.

Acute Pancreatitis diagnostic criteria in COVID-19:

It is important to make the correct diagnosis of AP in COVID-19 patients although it can be difficult. Just mere isolated rise in the pancreatic enzymes in a patient with COVID-19 shall not be attributed without clinico-radiological correlation to acute pancreatitis. The isolated raise of the enzymes can be can be seen in gastroenteritis and lung injury, especially in the presence of renal or respiratory failure; conditions commonly present in severe COVID-19 [15].

In our study we used the revised Atlanta classification to make the correct diagnosis with at least two of the following three criteria:

(1) typical abdominal pain,

(2) serum amylase or lipase > 3 times the upper normal limit,

(3) characteristic findings on diagnostic imaging;

As the accurate clinical evaluation of of acute abdomen pain cannot be done in

COVID-19 patients in severe case requiring intensive care unit care with ventilatory support, diagnostic imaging is of more importance.

Importance of detecting acute pancreatitis for surgeons

In both acute pancreatitis and COVID-19, the target organ of impact is either acute respiratory distress syndrome or acute renal failure when both are combined severity assessment and response assessment will become obscure. Occurrence of acute pancreatitis can aggravate the inflammatory response already induced by SARS-CoV-2 leading to accelerated organ failure [10].

The possible presence of SARS-CoV-2 in the pancreatic tissue is also a concern for the surgical team as there is a possibility that this virus could also be present in the (peri) pancreatic fluid and necrotic tissues.

Hence all cases of acute pancreatitis shall be evaluated

enzymatically and radiologically to rule out coincidence of COVID-19 and vice versa.

Cary home message

1. pancreas is un common but not immune to COVID-19 and it is less as compared to digestive tract involvement;
2. Isolated elevation of the pancreatic enzymes may be common but may not be due to acute pancreatitis in all the cases;
3. standard criteria (revised Atlanta) shall be used to make the diagnosis in COVID-19 patients
4. Acute pancreatitis in a patient with COVID-19, due to the diagnostic dilemma, possibility of common target organs(s) involvement and accelerated clinical course is a double-trouble for both the patient and surgeon.
5. During the interventional management of moderate / severe necrotising pancreatitis surgeons needs to be more careful as there is increased possibility of exposure to SARS-CoV-2 through drained fluid or necrotic pancreatic tissues during procedure [16].

Conclusions

The incidence of pancreatitis in patient having COVID -19 infections are relatively uncommon and in patients having pancreatitis the susceptibility to SARS COV-2 infection are more than the normal public. The presentation may differ with more enzymatic response than anatomical damage in earlier cases. The development pancreatitis is potentially dangerous as both can affect the same target organ lung and kidney. All cases of acute pancreatitis shall be evaluated for COVID-19 infection also to plan for treatment protocol and adhere to safety protocols. The possible association between COVID-19 and pancreas as they might be involved in the management of acute pancreatitis at some point of time during its course.

References

1. Zhang H, Kang Z, Gong H, *et al*, Digestive system is a potential route of COVID-19: an analysis of single-cell coexpression pattern of key proteins in viral entry process. Gut, 2020; 69:1010-8. doi:10.1136/gutjnl-2020-320953
2. Liu F, Long X, Zou W, *et al*. Highly ACE2 expression in pancreas may cause pancreas damage after SARS-CoV-2 infection. medRxiv. Google Scholar, 2020.
3. McNabb-Baltar J, Jin DX, Grover AS, *et al*. Lipase elevation in patients with COVID-19. American Journal of Gastroenterology. Google Scholar, 2020.
4. Sultan S, Altayar O, Siddique SM, Davitkov P, Feuerstein JD, Lim JK, *et al*. AGA Institute Rapid Review of the GI and Liver Manifestations of COVID-19, Meta-Analysis of International Data, and Recommendations for the Consultative Management of Patients with COVID-19. Gastroenterology. 2020; S0016–5085(20):30593-X. doi: 10.1053/j.gastro.2020.05.001. [CrossRef] [Google Scholar
5. Al Bendavid E, Mulaney B, Sood N, *et al*. COVID-19 antibody seroprevalence in SANTA Clara County California. medRxiv, 2020. Google Scholar medRxiv preprint doi: https://doi.org/10.1101/2020.04.14.20062463.this version posted April 30, 202
6. Aoysius MM, Thatti A, Gupta A, Sharma N, Bansal P, Goyal H, *et al*. COVID-19 presenting as acute pancreatitis. Pancreatology. 10.1016/.pan.2020.05.003, 2020.
7. Anand ER, Major C, Pickering O, Nelson M. Acute pancreatitis in a COVID-19 patient. Br J Surg. 2020; 107(27):e182. doi: 10.1002/bjs.11657. [Europe PMC free article] [Abstract] [CrossRef] [Google Scholar]
8. Hadi A, Werge M, Kristiansen KT, Pedersen UG, Karstensen JG, Novovic S, *et al*. Coronavirus Disease-19 (COVID-19) associated with severe acute pancreatitis: case report on three family members Pancreatology 5:S1424-3903(20)30147-2, 2020. doi: 10.1016/j.pan.2020.04.021
9. Kaafarani HMA, Moheb ME, Hwabejire JO, Naar L, Christensen MA, Breen K, *et al*. Gastrointestinal complications in critically ill patients with COVID-19. Ann Surg Publish Ahead of Print (May 1), 2020. 10.1097/SLA.0000000000004004
10. Wang F, Wang H, Fan J, Zhang Y, Wang H, Zhao Q. Pancreatic injury patterns in patients with COVID-19 pneumonia. Gastroenterology, 2020. 10.1053/j.gastro.2020.03.055
11. Banks PA, Bollen TL, Dervenis C, *et al*. Acute Pancreatitis Classication Working Group. Classication of acute pancreatitis--2012: revision of the Atlanta classication and denitions by international consensus. Gut. 2013; 62(1):102-11.
12. Liu F, Long X, Zhang B, Zhang W, Chen X, Zhang Z, *et al*. ACE2 expression in pancreas may cause pancreatic damage after SARS-CoV-2 infection. Clin Gastroenterol Hepatol Apr, 2020; 22:S1542-3565(20):30537–30531. doi: 10.1016/j.cgh.2020.04.040. [CrossRef] [Google Scholar]
13. Spinelli A, Pellino G. COVID-19 pandemic: perspectives on an unfolding crisis. Br J Surg, 2020. https:// bjssjournals.onlinelibrary.wiley.com/ doi/10.1002/bjs.11627
14. Morrison AR, Johnson JM, Ramesh M, Bradley P, Jennings J, Smith ZR, *et al*. Letter to the editor: acute hypertriglyceridemia in patients with COVID-19 receiving tocilizumab J Med Virol, 2020. doi: 10.1002/jmv.25907
15. de-Madaria E, Siau K, Cárdenas-Jaén K. Increased amylase and lipase in patients with COVID-19 pneumonia: don't blame the pancreas just yet! Gastroenterology. 2020; 21(20):30561-30568. 10.1053/j.gastro.2020.04.044
16. Coccolini F, Tartaglia D, Puglisi A, Giordano C, Pistello M, Lodato M, *et al*. SARS-CoV-2 is present in peritoneal fluid in COVID-19 patients. Ann Surg (in press), 2020. Retrieved fromhttps://journals.lww.com/annalsofsurgery/Documents/SARS-CoV-2%20is%20present%20in%20peritoneal%20fluid%20in%20COVID-19%20patients.pdf