Severity of Acute Pancreatitis in COVID Pandemic

Rahul Dhabalia, Vineet Chauhan**, Hardik Kakadiya**

Abstract

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the ongoing pandemic of coronavirus disease 2019 (COVID-19) and has caused more than 80 million infections and 1.7 million deaths worldwide. Although it is primarily a respiratory virus, SARS-CoV-2 also has extra-pulmonary effects. Pancreatic injury and cases of acute pancreatitis (AP) have been recognized and attributed to SARS-CoV-2. **Aim:** To study severity of Acute Pancreatitis during the covid pandemic as compared to a time period before the pandemic. **Methods:** A group of 100 patient diagnosed with acute pancreatitis between April 2020 to December 2020 (Group A) were compared with a group of 100 patients diagnosed with Acute Pancreatitis during the similar time frame in 2019 with respect to several parameters indicating the severity and complication rates of Acute Pancreatitis. **Results:** Revised Atlanta 2012 Grading, Ranson's score and Glasgow Criteriashowed significant difference in severity of acute Pancreatitis between the two groups ($p<0.05$). Patients with AP during COVID had higher severity as compared to before COVID.Patients with AP during COVID had significantly more ICU admission and significantly higher mortality and transient organ failure as compared to patients with AP before ICU. **Conclusion:** From the study, it has been found that Covid has impacted the health of the people and had some major issues. As target organs are same in severe AP and severe COVID19, acute respiratory distress syndrome or acute renal failure resulting from the latter can lead to inaccurate severity assessment. Acute pancreatitis in covid pandemic has affected the actions and activities of people.

Keywords: Acute pancreatitis, Covid, Pandemic, Respiratory disease

Introduction:

Coronavirus disease 2019 (COVID-19) emergence in December 2019 brought unprecedented challenges to global health care. Until December 28, 2020, more than 80 million cases had been confirmed globally and were responsible for more than 1.7 million deaths. The most common clinical manifestations of COVID-19 are respiratory, particularly fever and cough, but as cases have increased of widespread severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) across the globe, other symptoms and clinical scenarios have emerged. [1] Gastrointestinal (GI) and hepatic involvement, among others, have been recognized and are mediated by the expression of angiotensin-converting enzyme 2 (ACE2) on the GI tract, the main receptor of SARS-CoV-2. A recent systematic review and meta-analysis showed that the estimated prevalence of digestive symptoms is 15%. Nausea, vomiting, diarrhea, and loss of appetite are the most frequent symptoms. [2] Nineteen percent of patients present with liver injury, which may be more prevalent in fatal cases. Furthermore, approximately 10% of COVID-19-positive patients may present with only GI symptoms. This clinical presentation may be associated with the delayed diagnosis of COVID-19 and a tendency of the disease to progress to more severe forms.

The expression of ACE2 in pancreatic cells (both exocrine glands and islets) renders the pancreas a potential target for SARS-CoV-2, but only recently has it received attention for its role in the COVID-19

* Resident
** Assistant Professor
Department of General Surgery, B J Medical College, Ahmedabad, Gujarat
Correspondence : Dr. Vineet Chauhan
E-mail : drvineetchauhan@gmail.com

clinical picture. Several case reports of pancreatic injury and acute pancreatitis (AP) caused by the novel coronavirus have been reported. [3] About 1%-2% of non-severe and 17% of severe cases of COVID-19 exhibit pancreatic injury, which may have developed before the patient's admission.

SARS-CoV-2 infection requires entry of the virus into the host cell. Metallopeptidase ACE2 has been identified as the cell receptor. Transmembrane serine protease 2 (TMPRSS2) facilitates viral entry at the plasma membrane surface. As such, coexpression of both ACE2 and TMPRSS2 is critical for successful SARS-CoV-2 infection. [4] ACE2 is normally expressed in the pancreas. Ather explored its expression and distribution, finding higher levels of ACE2 in the pancreas than in the lung and ACE2 expression in both exocrine glands and islets. Most studies have focused on ACE2 expression and there are few reports on TMPRSS2 expression in the pancreas. [5] In one of these studies, Kandasamy, S.[6], found that ACE2 is mainly expressed in islet and exocrine tissue capillaries and some ductal cells, while TMPRSS2 is mainly expressed in ductal cells. [6] However, ACE2 and TMPRSS2 are rarely co-expressed in pancreatic ducts. Pancreatic beta cells do not co-express ACE2 and TMPRSS2 and several authors have questioned the direct cytotoxic effects of SARS-CoV-2 on beta cells. It is still unknown whether SARS-CoV-2 directly and/or indirectly affects beta cell function. [7]

Aims:

To study severity of Acute Pancreatitis during the covid pandemic as compared to a time period before the pandemic.

Methods:

It is a Retrospective observational study carried out at Civil Hospital, Ahmedabad. Two groups – Group A and Group B were defined. Group A consisted of 100 randomly selected patients diagnosed with Acute pancreatitis from April 2020 to December 2020. Group B consisted of 100 randomly selected patients diagnosed with Acutepancreatitis from April 2019 to December 2019. In both these groups, patients who presented to OPD/Emergency with clinical features suggestive of Acute pancreatitis such as Epigastric pain and vomiting and in ultrasonography diagnosed to be due to Acute pancreatitis were included in the study.

Inclusion criteria:

1.) All patients diagnosed on clinical picture and ultrasonography as Acute pancreatitis

Exclusion criteria:

1.) Past history of pancreatitis

Results:

For the study, different age group people were involved in the analysis. According to analysis, 100 people with mean age of 50.09 years evaluated before covid and 100 people with mean age of 51.07 years evaluated during covid.

For the study, both male and female participants were involved in the analysis. According to outcome of study, 43 females and 57 males and were observed before COVID and 52 females and 48 males were evaluated during the COVID.

There are various issues were identified among the patients during the COVID. As per the analysis, abdominal pain was found in patients before and during COVID. Total 177 patients were found with this issue. Here P>0.05 and show no significant difference in abdominal pain between groups.

Epigastric Tenderness is a serious issue that has direct impact on the physical and mental health of the individual. According to outcome of analysis, 144 patients were having such issue before and during covid. Here P=0.012 which is less than 0.05 and showing statistically significant difference in tenderness between groups.

Table 1: Level of Serum Amylase and Lipase

Variable	Period		Total	P value
	Before COVID	During COVID		
Lipase/amylase level>3x ULN at admission	34	72	106	<0.001
Lipase/amylase level <3x ULN at admission	66	28	94	
Total	100	100	200	

Revised Atlanta 2012 Grading showed significant difference in severity of acute Pancreatitis between the two groups (p<0.05). Patients with AP during COVID reported more severity as compared to before COVID.

Figure 1: Distribution of participants as per Revised Atlanta 2012 Grading

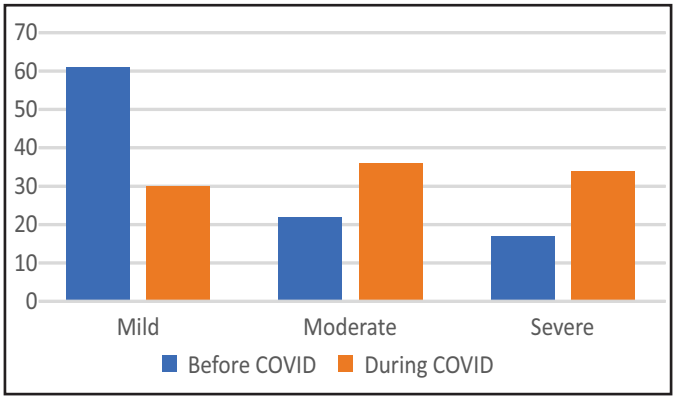
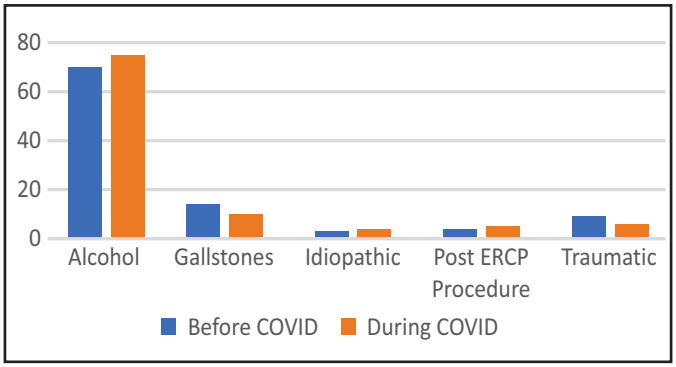


Figure 2: Distribution of various causes of acute pancreatitis among study participants



The most number of patients with Etiology were found related to Alcohol consumption . As per the analysis, 145 patients were having this issue before and during Covid. Apart from this, idiopathic was found in 7, Gall stones were found in 24, Post ERCP procedure were identified among 9 and Traumatic issues were observed in 15 patients. P=0.14 and hence shows significant difference in etiology between the groups.

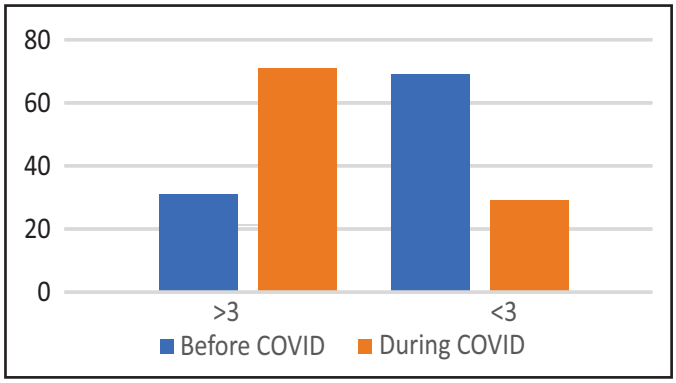
Table 2 : Distribution of Ranson's Score among study participants

Ranson's Score	Period		Total	P-value
	Before COVID	During COVID		
>3	33	71	104	0.03
<3	67	29	96	
Total	100	100	200	

There was significant difference in Ranson's score between the groups (p<0.05). Patients with AP during COVID had higher severity as compared to before COVID.

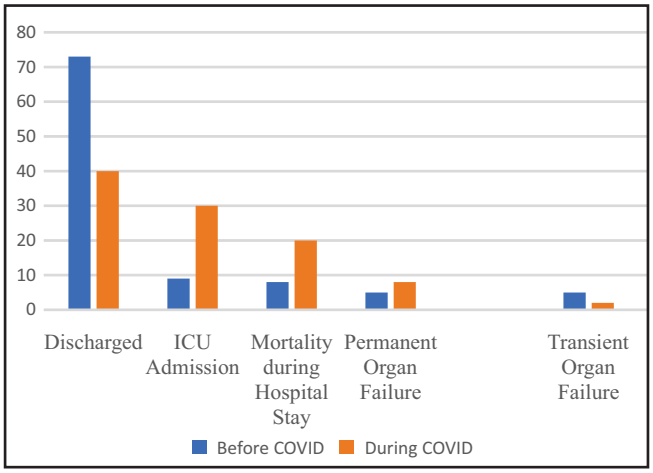
There was significant difference in Glasgow Criteria between the groups (p<0.05). Patients with AP during COVID had higher severity as compared to before COVID.

Figure 3: Distribution of Glasgow Criteria among study participants



The Clinical Outcome of the study shows there was a statistically significant difference between the two groups (p<0.05). Patients with AP during COVID had significantly more ICU admission and significantly higher mortality and transient organ failure as compared to patients with AP before ICU.

Figure 4: Clinical Outcome of study participants



Discussion:

Pancreatic lesions, usually defined by serum amylase and/or lipase elevations, and cases of AP have been reported in COVID-19 patients. Autopsy studies in patients previously infected by SARS-CoV-2 identified areas of focal pancreatitis and pancreatic and/or peripancreatic necrosis and calcifications, but only two-thirds of these patients had exhibited symptoms suggestive of AP. [8]

The **diagnosis of AP,** based on the **modified Atlanta criteria**, requires two of the following three features:

- Abdominal pain consistent with AP (acute onset of a persistent, severe, epigastric pain often radiating to the back)
- serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal
- Characteristic findings of AP on contrast-enhanced computed tomography (CECT) less commonly magnetic resonance imaging or transabdominal ultrasonography.

This classification also divides AP into interstitial edematous pancreatitis and necrotizing pancreatitis and identifies local and systemic complications, which have a clear impact on disease progression, morbidity, and mortality. [9] All cases included in our study fulfilled the above criteria for the diagnosis of Acute Pancreatitis. However, COVID-19-associated glucose metabolism changes and diabetes appear to be multifactorial, resulting from systemic inflammation and metabolic changes in other organs, including the liver, muscle and adipose tissues, and are not exclusively the result of pancreatic damage. Further studies evaluating SARS-CoV-2 entry into beta cells and not only receptor expression are needed. Severe cases of AP and COVID-19 are characterized by a cytokine storm, which ultimately leads to multiorgan failure and increased mortality. [10] The Clinical Outcome of the study shows that that there was statistically significant difference in outcome between the two groups.

A recent meta-analysis by Lakshmanan, and Malik,[11] found similar patterns of cytokine expression in both COVID-19 and AP. In this scenario, pancreatic damage may result in interstitial leakage of pancreatic lipase and consequently fat tissue lipolysis increasing unsaturated fatty acid levels, which in turn causes mitochondrial injury and excessive production and release of proinflammatory mediators–a cytokine storm. [11] Levels of interleukin IL-6, IL-8, and IL-10 were increased in severe cases of both AP and COVID-19 compared to nonsevere cases. Ranson's Score showed significant difference between the two groups. Consequently, some authors have hypothesized a beneficial role of extracorporeal cytokine absorption in severe cases. At this point, there are insufficient data to differentiate between severe AP caused by COVID-19 from severe AP with COVID-19. After the cytokine storm associated with severe COVID-19 cases, there is a migration of inflammatory cells to the inflammation/infection site, promoting a proinflammatory feedback loop. [12] Tissue factor is upregulated on platelets, white blood and endothelial cells, leading to activation of both extrinsic and intrinsic coagulation pathways and thrombin generation. This microthrombotic event described in lung vasculature can also take place in the pancreatic vasculature, causing hypoperfusion and ischemia with the subsequent induction of an inflammatory response and AP.

As target organs are same in severe AP and severe COVID-19, acute respiratory distress syndrome or acute renal failure resulting from the latter can lead to inaccurate severity assessment of AP and response assessment when "step-up" approach is adopted to deal with local complications. In addition, occurrence of AP can aggravate the inflammatory response already induced by SARS-CoV-2 leading to accelerated organ failure. [13] Possible presence of SARS-CoV-2 in the pancreatic tissue is also a concern for the surgical team. According to outcome of analysis, 144 patients were having such issue before and during covid. Here P=0.012 which is less than 0.05 and showing statistically insignificant difference for Epigastric Tenderness. As this virus has been detected in the peritoneal fluid with a load higher than in the respiratory tract, there is a possibility that this virus could also be present in the peri pancreatic fluid and necrotic tissues. In addition, viremia may not be directly related to the severity of symptoms, and all the patients, irrespective of the symptom's severity, could have viral load in the peritoneal fluid. [14] Although the possibility of viral load in pancreatic necrotic tissue and fluid is uncertain, interventions required to manage local complications (acute necrotic collections or walled off necrosis), whether percutaneous, endoscopic, or minimally invasive (retroperitoneal/ transperitoneal), might expose the health care workers to SARS-CoV-2, more so with high-risk aerosol generating procedures like endoscopic or minimally invasive drainage/necrosectomy including video-assisted retroperitoneal debridement (VARD). [15] In addition, it is unknown how long virus might persist in the peri pancreatic fluid or tissues that become relevant while managing symptomatic pseudocyst or walled-off necrosis once acute episode is over.

Conclusion:

From the study, it has been carried out that Covid has impacted the health of the people and had some major issues.As target organs are same in severe AP and severe COVID-19, acute respiratory distress syndrome or acute renal failure resulting from the latter can lead to inaccurate severity assessment of AP and response assessment when "step-up" approach is adopted to deal with local complications.Acute pancreatitis in covid pandemic has affected the actions and activities of people. The patients were having localized pain, diffused pain and Epigastric Tenderness. The Clinical Outcome of the study shows that there was statistically significant difference in outcome between the two groups.

References:

1. Inamdar, S., Benias, P.C., Liu, Y., Sejpal, D.V., Satapathy, S.K., Trindade, A.J. and Northwell COVID-19 Research Consortium, 2020. Prevalence, risk factors, and outcomes of hospitalized patients with coronavirus disease 2019 presenting as acute pancreatitis. Gastroenterology, 159(6), pp.2226-2228.
2. Hegyi, P., Szakács, Z. and Sahin-Tóth, M., 2020. Lipotoxicity and cytokine storm in severe acute pancreatitis and COVID-19. Gastroenterology, 159(3), pp.824-827.
3. Jones, C.M., Radhakrishna, G., Aitken, K., Bridgewater, J., Corrie, P., Eatock, M., Goody, R., Ghaneh, P., Good, J., Grose, D. and Holyoake, D., 2020. Considerations for the treatment of pancreatic cancer during the COVID-19 pandemic: the UK consensus position. British journal of cancer, 123(5), pp.709-713.
4. Dirweesh, A., Li, Y., Trikudanathan, G., Mallery, J.S., Freeman, M.L. and Amateau, S.K., 2020. Clinical outcomes of acute pancreatitis in patients with coronavirus disease 2019. Gastroenterology, 159(5), pp.1972-1974.
5. Lax, S.F., Skok, K., Zechner, P., Kessler, H.H., Kaufmann, N., Koelblinger, C., Vander, K., Bargfrieder, U. and Trauner, M., 2020. Pulmonary arterial thrombosis in COVID-19 with fatal outcome: results from a prospective, single-center, clinicopathologic case series. Annals of internal medicine, 173(5), pp.350-361.
6. Kandasamy, S., 2020. An unusual presentation of COVID-19: acute pancreatitis. Annals of Hepato-biliary-pancreatic Surgery, 24(4), pp.539-541.
7. Dhar, J., Samanta, J. and Kochhar, R., 2020. Corona virus disease-19 pandemic: the gastroenterologists' perspective. Indian Journal of Gastroenterology, pp.1-12.
8. Singh, A.K., Gupta, R., Ghosh, A. and Misra, A., 2020. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 14(4), pp.303-310.
9. Bokhari, S.M.M.A. and Mahmood, F., 2020. Case Report: Novel Coronavirus—A Potential Cause of Acute Pancreatitis?. The American Journal of Tropical Medicine and Hygiene, 103(3), p.1154.

10. Stevens, J.P., Brownell, J.N., Freeman, A.J. and Bashaw, H., 2020. COVID-19-Associated multisystem inflammatory syndrome in children presenting as acute pancreatitis. Journal of pediatric gastroenterology and nutrition, 71(5), pp.669-671.

11. Lakshmanan, S. and Malik, A., 2020. Acute pancreatitis in mild COVID-19 infection. Cureus, 12(8).

12. Gupta, V., 2020. COVID-19 and acute pancreatitis: what do surgeons need to know?. Indian Journal of Surgery, 82, pp.301-304.

13. Miró, Ò., Llorens, P., Jiménez, S., Piñera, P., Burillo-Putze, G., Martín, A., Martín-Sánchez, F.J., Lamberechts, J., Alquézar-Arbé, A., Jacob, J. and Noceda, J., 2020. A case-control emergency department-based analysis of acute pancreatitis in Covid-19: Results of the UMC-19-S6. Journal of Hepato-Biliary-Pancreatic Sciences.

14. Hadi, A., Werge, M., Kristiansen, K.T., Pedersen, U.G., Karstensen, J.G., Novovic, S. and Gluud, L.L., 2020. Coronavirus disease-19 (COVID-19) associated with severe acute pancreatitis: case report on three family members. Pancreatology, 20(4), pp.665-667.

15. Chiarello, M.M., Cariati, M. and Brisinda, G., 2020. Assessment of severity of acute pancreatitis in a Sars-CoV-2 pandemia. The British Journal of Surgery.