

Favipiravir Induced Acute Pancreatitis in a COVID-19 Patient

AHM Ejrarul Alam Khan¹, Mohammad Mahfuzul Hoque², Md Uzzwal Mallik³, Kamalesh Chandra Basu⁴, Mohammed Masudul Hasan⁵, Imran Mahmud⁶, Mirza Mohammad Asif Adnan⁷, Md Mujibur Rahman⁸

Abstract:

There are a number of gastrointestinal symptoms and complications of COVID-19. Asymptomatic increase in pancreatic enzymes and rarely symptomatic pancreatitis are observed in this disease. This article describes a 37-year-old male suffering from mildly symptomatic COVID-19 infection, who received tablet favipiravir for his management. His condition was improving, when he developed acute pancreatitis, diagnosed clinically, biochemically and also with help of abdominal ultrasound. When he developed this, all typical symptoms of COVID-19 were improved. As a result, role of favipiravir in the development of this pancreatitis was suspected.



DOI: <https://doi.org/10.3329/jom.v22i1.51396>

Copyright: © 2021 This is an open access article published under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited, is not changed in any way and it is not used for commercial purposes.

Received: 02 December, 2020;

Accepted: 10 December, 2020

Background:

COVID-19 infection was declared a global pandemic by WHO in early part of the year 2020. Common presentations of this infection are fever, cough, fatigue, shortness of breath, sore throat, headache, myalgias, etc. (1) There are also some gastrointestinal symptoms like diarrhea, anorexia, gastrointestinal bleeding, elevated level of liver enzymes, etc. There are some reports of elevated blood levels of pancreatic enzymes, most of cases not associated with clinical or radiological evidence of acute pancreatitis. (2) There are

some case reports of acute pancreatitis in relation to COVID-19 infection. Here, we present a 37-year-old male, with no prior risk factors of pancreatitis, suffering from mild symptomatic COVID-19 infection, later developing acute pancreatitis with complications. We are suspecting iatrogenic acute pancreatitis, where tablet Favipiravir may be a culprit agent.

Case:

A 37-year-old male, a known diabetic, nonsmoker, nonalcoholic, hailing from Faridpur, Bangladesh, was presented to local health facility with complaints of low grade fever, throat pain and mild dry cough for 3 days. There was no history of any abdominal pain, diarrhea, chest pain, bodyache or headache. His diabetes was well controlled with regular intake of metformin 500mg twice daily. He was advised for nasopharyngeal swab for RT-PCR for SARS-CoV-2, which came out positive after 3 days. His fever abated and other symptoms disappeared when he got the positive report. After getting the report he rushed to local health facility. He was advised to take several medications and he started tablet Favipiravir, along with Paracetamol, Fexofenadine, Montelukast, Famotidine and Vitamin B and C supplementation. Favipiravir was advised to take as 1600 mg stat dose, followed by 600 mg twice daily for 7 days.

Initial six days of favipiravir intake was uneventful but on

1. Medical officer, Dhaka Medical College Hospital, Dhaka.
2. Assistant Professor, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
3. Assistant Professor, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
4. Assistant Professor, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
5. Assistant Professor, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
6. Registrar, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
7. Assistant registrar, Department of Medicine, Dhaka Medical College Hospital, Dhaka.
8. Professor of Medicine, Dhaka Medical College Hospital, Dhaka.

Corresponding author: Dr. AHM Ejrarul Alam Khan, Medical officer, Dhaka Medical College Hospital, Dhaka.

7th day (02/08/2020) he suddenly developed severe abdominal pain, which was mostly in the epigastric region, radiated into the back. Then he developed vomiting for several episodes, not associated with any hematemesis or diarrhea, followed by gradual distension of abdomen and constipation. His urine volume and colour was normal. He also developed altered conscious level and incoherent speech. There was no history of convulsion, headache, and fever. He was referred to Dhaka Medical College Hospital (DMCH), Dhaka for further management.

He was admitted in DMCH on 06/08/2020. He was slightly disoriented, with incoherent speech, GCS was 14/15. His pulse was 105/min, blood pressure was 90/70 mm Hg and temperature was 98^o F. His oxygen saturation was normal. Abdomen was distended, without any organomegaly. Moderate ascites was present with sluggish bowel sound. Other system examination revealed no abnormality.

On admission, he was diagnosed as a case of Acute Pancreatitis with Acute Kidney Injury. There was also low hemoglobin level and mild hyponatremia and hypocalcemia (Table 1). Fasting lipid profile was also normal.

He had an ultrasonography of whole abdomen, which showed swollen and mildly edematous pancreas with homogeneous echotexture, with mild hepatomegaly and moderate ascites. In plain X-ray abdomen there were multiple air fluid levels at small bowel.

He was treated conservatively, at first nothing per os, with intravenous fluid supplementation, injectable antibiotic (Injection Meropenem and Moxifloxacin), injectable omeprazole and analgesic. He also received injection enoxaparin, 40 mg, subcutaneously, twice daily. His abdominal pain gradually improved and constipation relieved. His bowel sound became normal and abdominal distension also improved, while he was allowed oral food. After 2 days his serum creatinine reached 6.79 mg/dL and later his renal function started improving without requiring any dialysis. He was discharged on 19/08/2020, when his general well-being was restored, renal function became almost normal and there was no abdominal complaint. This whole duration, he did not need any supplemental oxygen or any invasive procedures including dialysis. He was discharged with advice of reviewing in Post-Acute Care Clinic for COVID-19 in DMCH with renal function

Table 1. Investigation findings

Investigations	Results
• Complete blood count	
Hemoglobin	9 g/dL
Total count of WBC	7.56×10 ⁹ /L
Neutrophil	89%
Lymphocytes	7.7%
Eosinophil	0%
Monocytes	3.3%
Basophil	0%
Platelet count	139×10 ⁹ /L
• S. Creatinine	7.33 mg/dL
• S. Electrolytes	
Sodium	129 mmol/L
Potassium	4.6 mmol/L
Chloride	89 mmol/L
• SGPT	18 U/L
• SGOT	48 U/L
• C reactive protein	<6 mg/L
• S. Lipase	299 U/L
• S. Calcium	6.70 mg/dL
• Fasting lipid profile	
Total cholesterol	138 mg/dL
Triglyceride	127 mg/dL
LDL cholesterol	101 mg/dL
HDL cholesterol	38 mg/dL
• Ultrasonography of whole abdomen	<ul style="list-style-type: none"> • Swollen and mildly edematous pancreas with homogeneous echotexture • Mild hepatomegaly • Moderate ascites

tests. He reported to Post-Acute Care Clinic with full recovery.

Discussion:

In this case, we discussed about a middle aged diabetic gentleman, who developed acute pancreatitis complicated by acute kidney injury, about 14 days after the onset of fever, while he was completely afebrile and no typical COVID-19 symptoms were present at that time. He developed this complication 7 days after starting of tablet Favipiravir. He never needed any oxygen support and his condition developed with conservative management.

There are a number of symptoms and complications of COVID-19. The most characterized symptoms of COVID-19 are fever, cough, fatigue, dyspnea, sore throat, headache, and myalgias or arthralgias. Approximately 80 % of patients demonstrate mild symptoms; 20 % have severe disease; about 5% of patients exhibit critical disease symptoms such as respiratory arrest, septic shock, or multiple organ failure¹. There are a number of gastrointestinal, hepatobiliary and pancreatic symptoms and complications. Pan L et al showed in their descriptive cross sectional multicenter study that approximately 50% of patients had symptoms such as diarrhea, nausea, vomiting, abdominal pain, etc.³. There were also case reports of COVID-19 patients presenting with gastrointestinal bleeding. A number of patients were noted to have liver injury, ranging from mild to severe². But clinical pancreatitis is not much common. Though a study by Wang et al. examining 52 patients with COVID-19 pneumonia, 17 % of patients experienced pancreatic injury, defined by any abnormality in amylase or lipase, they did not exhibit clinical symptoms of severe pancreatitis. But it should be noted that the ACE2 receptor is highly expressed in pancreatic islet cells, therefore theoretically islet cells damage can be caused by COVID-19 infection⁴.

Later a number of case reports were found where acute pancreatitis was associated with COVID-19 infection. In most of them pancreatitis was present at the time of presentation and the presentation of COVID 19 was severe, requiring oxygen support. Aloysius M et al reported a case where a 36-year-old obese female, who presented with severe acute pancreatitis along with other symptoms of COVID-19, who required ICU admission and high flow oxygen support due to ARDS (5). Hadi et al. reported familial clustering of COVID-19 cases with two of three family members with COVID-19 had acute pancreatitis. One of these cases had no abdominal symptoms but had rising pancreas specific serum amylase levels that warranted further investigation, and diagnosis of acute pancreatitis was made on ultrasonography that showed inflamed edematous pancreas without gallstones⁶. But Anand et al. reported a case of COVID-19 who initially presented with fever, cough, sore throat and myalgia. Patient recovered from this illness but presented again with abdominal symptoms 5 days after the discharge. Later, acute pancreatitis was diagnosed on CT scan that showed diffusely edematous pancreatitis. Authors considered this might be idiopathic in nature in this case, but also suspected causal relationship between COVID-19 and acute pancreatitis due to their temporal association⁷.

In our case, patient had mild symptoms of COVID-19, but almost completely recovered, when he developed acute

pancreatitis. He had mild features of COVID-19 pneumonia, maintaining his oxygen saturation in normal limit in the whole period. We are suspecting that his acute pancreatitis may be secondary to the medication Favipiravir, though we did not find any published case reports of pancreatitis due to favipiravir. But as his COVID-19 symptoms are mild, and he was recovering while he developed acute pancreatitis, there was no prior risk factor for acute pancreatitis and there is a temporal relationship between development of acute pancreatitis and ingestion of Favipiravir, we are suspecting that Favipiravir might be the culprit here, though further investigations are suggested.

Conclusion:

Though research is ongoing regarding a number of drugs for treatment for COVID-19, most of them are yet to be proven effective. However, many drugs are being prescribed for treatment for COVID-19 without clear indications. In many cases, these may cause more harm than good. In this report, we tried to elaborate the fact that caution should be exercised in prescribing any medication in COVID-19 without any definite indications.

References:

1. Buruk K, Ozlu T. New Coronavirus: SARS-COV-2. *Mucosa*. 2020;1–4. Doi:10.33204/mucosa.706906.
2. Pan L, Mu M, Ren HG, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional multicenter study. *Am J Gastroenterol* 2020;115:766–773. Doi: 10.14309/ajg.0000000000000620
3. Patel KP, Patel PA, Vunnam RR, et al. Gastrointestinal, hepatobiliary, and pancreatic manifestations of COVID-19. *J Clin Virol* 2020;128:128. Doi:10.1016/j.jcv.2020.104386
4. Wang F, Wang H, Fan J, Zhang Y, Wang H, Zhao Q, Pancreatic injury patterns in patients with COVID-19 pneumonia, *Gastroenterology* (2020), Doi: 10.1053/j.gastro.2020.03.055.
5. Aloysius M, Thatti A, Gupta A. COVID-19 presenting as acute pancreatitis. *Pancreatolgy*. 2020: 1026-1027. Doi: 10.1016/j.pan.2020.05.003
6. 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. *Pancreatolgy*. 2020:665-667. Doi: 10.1016/j.pan.2020.04.021
7. Anand ER, Major C, Pickering O, Nelson M. Acute Pancreatitis in a COVID-19 Patient. *Br J Surg* 2020; 107: e182. Doi: 10.1002/bjs.11657.