

## CASE REPORT

# COVID-19 treatment: A potential cause of acute pancreatitis

Magdy Mohamed Allam<sup>1,2</sup>  | Hanaa Tarek El-Zawawy<sup>3</sup>  | Soha Magdy Ahmed<sup>4</sup>  | Mohamed Aly Abdelhamid<sup>5</sup>

<sup>1</sup>Lecturer of Endocrinology, Alexandria University Students' Hospital, Alexandria, Egypt

<sup>2</sup>Consultant of Endocrinology, Zulekha Hospital, Dubai, United Arab Emirates

<sup>3</sup>Assistant Professor of Endocrinology, Alexandria University Faculty of Medicine, Alexandria, Egypt

<sup>4</sup>Consultant of Diabetes and Endocrinology, Alexandria University Students' Hospital, Alexandria, Egypt

<sup>5</sup>Critical Care Department, Alexandria University, Alexandria, Egypt

## Correspondence

Magdy Mohamed Allam, Lecturer of Endocrinology, Alexandria University Students' Hospital, Alexandria, Egypt. Email: [drmagdyallam@gmail.com](mailto:drmagdyallam@gmail.com)

## Abstract

Remdesivir can precipitate fatal acute necrotizing pancreatitis especially in patients who previously suffer from hypertriglyceridemia.

## KEYWORDS

COVID-19, hypertriglyceridemia, pancreatitis, remdesivir

## 1 | INTRODUCTION

The novel RNA coronavirus responsible for the coronavirus disease-19 (COVID-19) pandemic has much impacted people's health all over the world. The clinical manifestations of COVID-19 are variable, ranging from asymptomatic cases to severe respiratory affection. Also, COVID-19 and its treatment were found to induce or exacerbate other diseases.<sup>1</sup>

Remdesivir (GS-5734), an inhibitor of the viral RNA-dependent, was identified as a promising therapeutic candidate for COVID-19 because of its ability to inhibit SARS-CoV-2 in vitro and to reduce lung viral load and lung damage.<sup>2</sup>

Patients with COVID-19 are characterized by having elevated serum triglycerides level which is known to

be associated with a poor prognosis. Patients with low COVID-19 positive-to-negative transmission were found to have higher serum triglycerides, which can be a sign of severity.<sup>3</sup>

We demonstrate 2 cases who suffered from hypertriglyceridemia and acute pancreatitis after receiving Remdesivir during the treatment of COVID-19 infection.

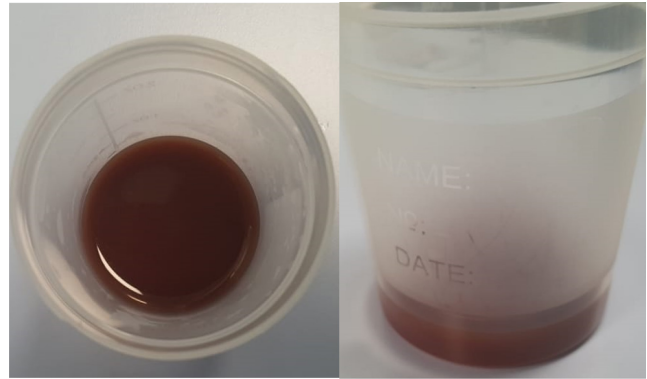
## 2 | CASE PRESENTATION

### 2.1 | Case one

A 35-year-old Indian male patient presented to the emergency department (ER) on the September 9, 2021, with fever and cough, he did not complain of chest pain or shortness of breath. The patient received 2 doses of Pfizer

vaccine 2 months prior to his symptoms. His past medical history included familial hypertriglyceridemia and type 2 diabetes and was maintained on sitagliptin 50mg and metformin 500mg. Clinical examination showed: heart rate (HR): 109 beats per minute (BPM), respiratory rate (RR): 20 cycles/min, temperature: 38°C, blood pressure (BP): 120/80 mmHg, and SPO<sub>2</sub>: 97%. His laboratory investigations were as follows: COVID-19 PCR: positive, triglycerides: 500 mg/dL (<150), random blood sugar (RBS): 279, SGOT: 136.4 U/L (8–45), SGPT: 136.7 U/L (0–35), total bilirubin: 0.55 mg/dL (0.1–1.2), CRP: 35 mg/L (0–5), and lactate: 3.5 mmol/L (0.5–2.2). The complete blood count (CBC) showed lymphopenia. Abdomen X-ray showed fecal loading of ascending and descending colon and patchy opacities in lower lung zones bilaterally. CT scan of the chest showed bilateral pneumonitis, patchy consolidations with peri bronchial thickening and bilateral posterior basal pleural thickening with atelectasis. The patient was diagnosed with COVID-19 induced pneumonia and was admitted to the ICU. He received Remdesivir (200 mg IV loading dose on the first day then 100mg IV maintenance dose for 2 days). The patient's condition improved gradually, and he was discharged after 10 days.

Four days after his discharge, the patient presented to the ER with fever, severe epigastric abdominal pain, and constipation. Clinical examination showed: HR: 131 BPM, RR: 22 cycle/min., temperature 38.5°C, BP 100/53 mmHg, and SPO<sub>2</sub> 94%. The patient was in severe pain, with tenderness all over the abdomen, distended abdomen, and decreased bowel sounds. His laboratory results were as follows: COVID-19 PCR: negative; triglycerides: 1569.9 mg/dL (<150), amylase: 1127 U/L (28–100), lipase: 2927 U/L (<60), CRP: 41.40 mg/L (0–5), procalcitonin: 0.139 ng/mL (0–0.049), lactate: 3.5 mmol/L (0.5–2.2), coagulation profile and thyroid function tests were unremarkable. However, urea, blood urea nitrogen (Bun), creatinine, serum calcium, glucose random, sodium, potassium, chloride, phosphorus, and creatinine bilirubin total, bilirubin direct, SGOT, SGPT, alkaline phosphatase, total proteins, albumin, and lipid profile could not be assessed because the sample was heavily lipemic. CT scan of the abdomen showed acute pancreatitis and diffuse reversible acute intestinal ischemia. The patient was diagnosed with acute necrotizing pancreatitis secondary to hypertriglyceridemia and was admitted to the ICU. He received the following medications daily: IV fluids, teicoplanin 400 mg, meropenem 1 gm, levofloxacin 500 mg, metronidazole 500 mg, albumin, IV paracetamol 1 gm, IV pantoprazole 40 mg, tramadol 100 mg IV, omega 3 1 gm, fenofibrate 145 mg, atorvastatin 20 mg, IV morphine 4 mg, insulin according to sliding scale, enoxaparin 40 mg SC injection, IV ondansetron, IV hydrocortisone. Laboratory investigations 2 days later showed: COVID-19



**FIGURE 1** Ascitic fluid aspirate during acute peritonitis

PCR: positive, triglycerides: >5000 mg/dL (<150), procalcitonin: 3.290 ng/mL (0–0.049), amylase: 1384 U/L (28–100), lipase: 1075 U/L (<60), CRP: 75.60 mg/L (0–5), His blood counts were as follows: hemoglobin (Hb): 12.2 g/dL, platelets (PLT):  $151 \times 10^9/L$ , and white blood cells (WBC):  $20.3 \times 10^9/L$ . Troponin T HS 8.9, lactate: >15.5 mmol/L (0.5–2.2), ABG: Ph 6.7, Pco<sub>2</sub> 69.1 mmHg, HCO<sub>3</sub> 8.4 mmol/L, and virology was negative (HIV, HBS Ag, and HCV Ab). The patient then developed moderate ascites and a right iliac fossa pigtail drain was placed successfully. After 2 days, the patient's condition deteriorated, and he was put on mechanical ventilation shortly. Two sessions of plasmapheresis were done; however, acute peritonitis was developed. The aspirated ascitic fluid was positive for amylase and lipase (Figure 1).

## 2.2 | Case two

A 68-year-old female Egyptian patient, presented to the ER with fever and cough on February 5, 2022. Clinical examination showed the following: HR: 100 BPM, RR: 16 cycle/min, temperature 37.8°C, BP 150/90 mmHg, and SPO<sub>2</sub> 94%. Laboratory investigations were as follows: COVID-19 PCR: positive, triglycerides: 130 mg/dL (<150), D-dimer: 70 ng/mL (<250 ng/mL), CRP: 6.1 mg/L (0–5), random blood sugar (RBS): 300 mg/dL and her blood counts were as follows: Hb: 11 g/dL, PLT:  $340 \times 10^9/L$ , and WBC:  $9.89 \times 10^9/L$ . The patient did not receive any COVID-19 vaccines. Her past medical history included type 2 diabetes, hypertension, dyslipidemia, and gout. Her drug history included the following: insulin glargine, vildagliptin 50 mg, metformin 500 mg, rosuvastatin 10 mg, febuxostat 40 mg, bisoprolol 5 mg, amlodipine 10 mg, and valsartan 160 mg. Surgical history included cholecystectomy 20 years ago. The patient was diagnosed with COVID-19 and was admitted to the hospital. She was prescribed the following medications: levofloxacin 500 mg, Vitamin C, antitussive medication, dexamethasone 8 mg

IV, and favipiravir 200 mg; 8 tablets/12 hours on Day 1, followed by 3 tablets/12 hours from Day 2 to Day 5. The patient improved and the fever subsided by the 3rd day.

On the 5th day, the temperature started rising again to 37.5°C. On the 8th day, the temperature increased to 38°C and the patient had high blood sugar levels and SPO2 decreased to 92%. Laboratory investigations showed: Triglycerides: 550 mg/dL (<150), SGOT: 78 U/L (8–45), SGPT: 66 U/L (0–35), amylase: 143 U/L (28–100), lipase: 186 U/L (<60), D-dimer: 307 ng/mL (<250 ng/mL), CRP: 5.5 mg/L (0–5), LDH: 152 U/L (132–214), urea: 51 mg/dL (<71), creatinine: 1.23 mg/dL (0.5–0.9), and BUN: 23 mg/dL (6–23). Remdesivir was started at a dose of 200 mg IV infusion on the first day and then a dose of 100 mg IV infusion for 4 days and the patient was started on an insulin basal bolus regimen.

After the end of the antiviral regimen (4 days later), the patient started complaining of severe abdominal pain radiating to the right side. Her laboratory investigations showed the following: Amylase: 169 U/L (28–100), lipase: 545.5 U/L (<60), D-dimer: 460 ng/mL (<250 ng/mL), and CRP: 15 mg/L (0–5). CT abdomen was performed, and results as shown in Figure 2. The patient was diagnosed with acute pancreatitis and was maintained on IV fluids, ursodeoxycholic acid, and nothing per mouth (NPO). After 6 days, the pain improved and pancreatic enzymes decreased; amylase: 121 U/L (28–100), lipase: 178 U/L (<60), and the patient was started on a soft diet. After 6 days, pancreatic enzymes further decreased; amylase: 90 U/L (28–100), lipase: 60 U/L (<60), and the patient's

clinical condition improved significantly, and she was discharged from the hospital.

### 3 | DISCUSSION

Studies on the side effects of COVID-19 treatment regimens are still deficient. We demonstrated in our 2 case presentations a serious effect of Remdesivir, an antiviral which has been approved in several countries to be used in hospitalized COVID-19 patients, on serum triglycerides. Such an effect of increased serum triglycerides could be fatal as the patient may die from acute pancreatitis rather than the COVID-19 infection itself.

Some studies showed that antiviral treatment in general is associated with hypertriglyceridemia.<sup>4</sup> On the contrary, other studies showed no effect of directly acting antiviral (DAA) therapy on triglyceride levels.<sup>5</sup>

In case 1, the patient suffered from severe hypertriglyceridemia and acute pancreatitis 4 days after finishing the antiviral therapy (Remdesivir) and being discharged from the hospital. This could be explained as an effect of Remdesivir that caused highly elevated serum triglycerides. And since the patient already suffered from familial hypertriglyceridemia and was having high serum triglycerides before catching the COVID-19 infection, this possibly augmented the condition and resulted in the shooting of serum triglycerides. Acute necrotizing pancreatitis was developed leading to death in our patient after the failure of all measures to lower serum triglycerides.

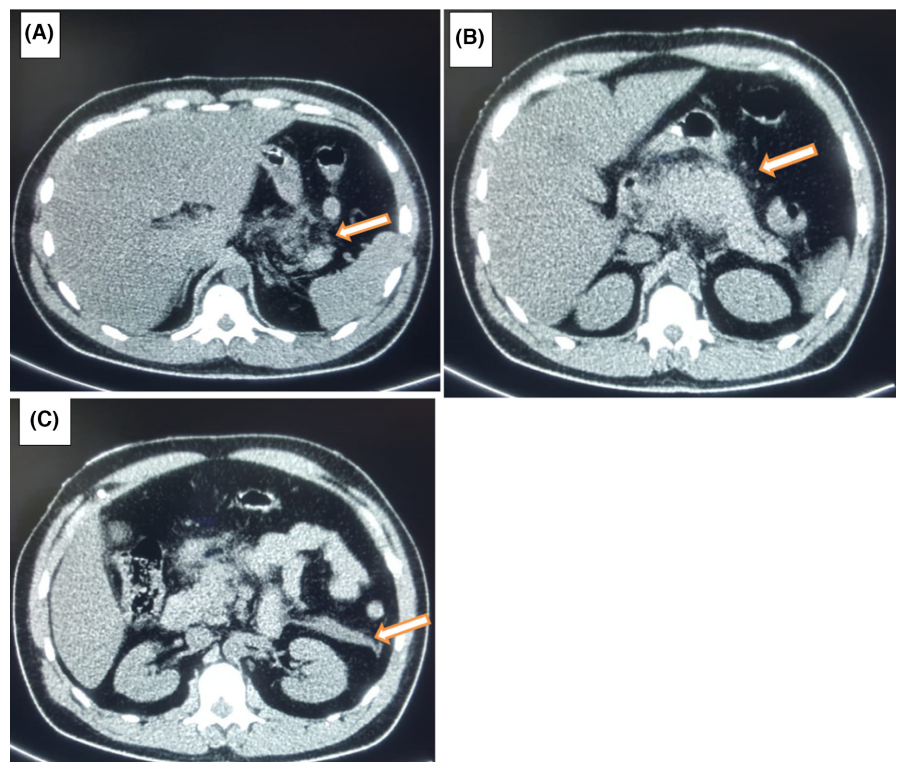


FIGURE 2 CT Abdomen axial view showing acute necrotizing pancreatitis

In case 2, the patient suffered from acute pancreatitis a few days after starting the antiviral regimen (Remdesivir). The patient had elevated serum triglycerides, elevated serum amylase, and lipase. The patient was diagnosed with acute pancreatitis, received the appropriate measures, and her condition was improved.

Aiming to identify the cause of acute pancreatitis in both patients, an extensive history and workup were done to eliminate other causes of acute pancreatitis (including alcohol, cholelithiasis, drugs, and viral induced pancreatitis). The markedly elevated serum triglycerides, amylase, and lipase confirmed the diagnosis of hypertriglyceridemia-induced pancreatitis.<sup>6</sup> The normal triglycerides level prior to treatment with Remdesivir could explain the moderately elevated triglycerides following Remdesivir and the difference between the course of pancreatitis in both cases.

Colipa proposed an approach to identify level of causal relationship of drug-induced adverse effects. This method of assessment is based on the analysis of five key elements. They include reaction time to onset in relation to drug, course of the reaction, re-exposure to the drug, and evocativeness/likelihood of symptoms (including expectedness of reaction and other factors may be involved). After reviewing previous cases, we found that Remdesivir is “*likely*” to induce acute pancreatitis through elevation of serum triglycerides. The chronological compatibility and relevant investigations were well established in both cases, however, rechallenge test was not performed.<sup>7</sup>

Data on the effect of Remdesivir on serum triglyceride levels and pancreatitis are still lacking. However, according to a signal published in the WHO Pharmaceutical Newsletter, treatment with Remdesivir appears to be associated with pancreatitis.<sup>8</sup> In agreement with our finding, we found only one very recently published article in the literature which was a retrospective analysis of COVID-19 patients treated with remdesivir in Japan. Miyazaki et al,<sup>9</sup> showed that there is an increased risk of acute pancreatitis or a higher increase in pancreatic enzyme levels in association with Remdesivir administration during COVID-19 treatment.

Remdesivir used in COVID-19 treatment could be the cause of elevated serum triglycerides with a potential risk for acute pancreatitis. Hence, we recommend that serum triglyceride levels be measured in all patients with COVID-19 prior to Remdesivir therapy. And we suggest that Remdesivir not be used in patients with hypertriglyceridemia. Further multifaceted large prospective studies should be conducted in this context to prove our suggestion.

## 4 | CONCLUSION

Remdesivir used in the treatment of COVID-19 infection may induce acute pancreatitis through elevation of serum triglycerides. Measuring serum triglycerides is likely to be important in patients with COVID-19 infection before starting Remdesivir therapy.

### AUTHOR CONTRIBUTIONS

**Allam MM** was responsible for data collection, interpretation & analysis, and critically reviewed the manuscript. **El-Zawawy HT** was responsible for data interpretation and analysis, participated in writing the manuscript, and critically reviewed the manuscript. **Ahmed SM** was responsible for writing the manuscript, participated in data analysis, and critically reviewed the manuscript.<sup>10</sup>

### ACKNOWLEDGMENTS

This research did not receive any specific grant funding from any agency in the public, commercial, or nonprofit sector.

### FUNDING INFORMATION

No sources of funding were declared for this study.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### DATA AVAILABILITY STATEMENT

Data are available on request due to privacy/ethical restrictions.

### ETHICAL AND CONSENT STATEMENT

A written informed consent was obtained from the patients to publish this report in accordance with the journal's patient consent policy.

### ORCID

Magdy Mohamed Allam  <https://orcid.org/0000-0003-3178-0487>

[org/0000-0003-3178-0487](https://orcid.org/0000-0003-3178-0487)

Hanaa Tarek El-Zawawy  <https://orcid.org/0000-0002-2778-7689>

[org/0000-0002-2778-7689](https://orcid.org/0000-0002-2778-7689)

Soha Magdy Ahmed  <https://orcid.org/0000-0002-1807-9250>

[org/0000-0002-1807-9250](https://orcid.org/0000-0002-1807-9250)

### REFERENCES

1. Allam MM, El-Zawawy HT, Ahmed SM, Aly AM. Thyroid disease and covid-19 infection: case series. *Clin Case Rep*. 2021;9(6):e04225.
2. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 - final report. *N Engl J Med*. 2020;383(19):1813-1826.



3. Wang L, Zhang Y, Cheng Y, et al. Serum triglyceride level and hypertension are highly associated with the recovery of COVID-19 patients. *Am J Transl Res*. 2020;12(10):6646-6654.
4. Imarhiagbe FA, Kubeyinje EP. Hypertriglyceridemia in antiretroviral therapy. *J Int AIDS Soc*. 2005;7(3):65.
5. Villani R, Di Cosimo F, Romano AD, Sangineto M, Serviddio G. Serum lipid profile in HCV patients treated with direct-acting antivirals: a systematic review and meta-analysis. *Sci Rep*. 2021;11(1):13944.
6. Sezgin O, Özdoğan O, Yaraş S, Üçbilek E, Altıntaş E. Evaluation of hypertriglyceridemia-induced acute pancreatitis: a single tertiary care unit experience from Turkey. *Turk J Gastroenterol*. 2019;30(3):271-277.
7. Bons B, Audebert F, Bitaudeau C, et al. Assessment of undesirable events in cosmetic market surveillance: background, description and use of a causality assessment method in cosmetovigilance. *Regul Toxicol Pharmacol*. 2010;58(3):349-353.
8. Rocca E. *Remdesivir and Pancreatic Toxicity WHO Pharmaceuticals Newsletter*. 2021; 3:16–21. Available from: URL: <https://www.who.int/publications/i/item/who-pharmaceuticals-newsletter---n-3-2021>
9. Miyazaki K, Yoshimura Y, Miyata N, et al. Acute pancreatitis or severe increase in pancreatic enzyme levels following remdesivir administration in COVID-19 patients: an observational study. *Sci Rep*. 2022;12(1):5323.

**How to cite this article:** Allam MM, El-Zawawy HT, Ahmed SM, Abdelhamid MA. COVID-19 treatment: A potential cause of acute pancreatitis. *Clin Case Rep*. 2022;10:e06465. doi: [10.1002/ccr3.6465](https://doi.org/10.1002/ccr3.6465)