CASE REPORT

Delayed Impact of COVID-19 on Diabetes

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ABSTRACT

Introduction: Active COVID-19 illness can worsen glycemic control and induce diabetes-related complications such as diabetic ketoacidosis (DKA) in patients with prediabetes and diabetes. There is a lack of available research and data for cases of delayed diabetic complications secondary to COVID-19. We report two cases of COVID-19 induced worsening of diabetic disease with a delayed onset including DKA and deteriorating glycemic control.

Case Presentation: Patient-A is a 28-year-old Hispanic male with a history of prediabetes controlled with diet and exercise. He was diagnosed with DKA approximately 10 weeks following his COVID-19 illness and recovery. At the time of the DKA diagnosis, his HbA1c was 11.6%. Prior to his COVID-19 illness, his HbA1c was 5.6%. Patient-B is a 63-year-old white male with type 2 diabetes. He was diagnosed with worsening peripheral neuropathic pain one month following COVID-19 illness. Prior to COVID-19, his HbA1c was 7.5% compared to 10.3% two months post COVID-19 illness.

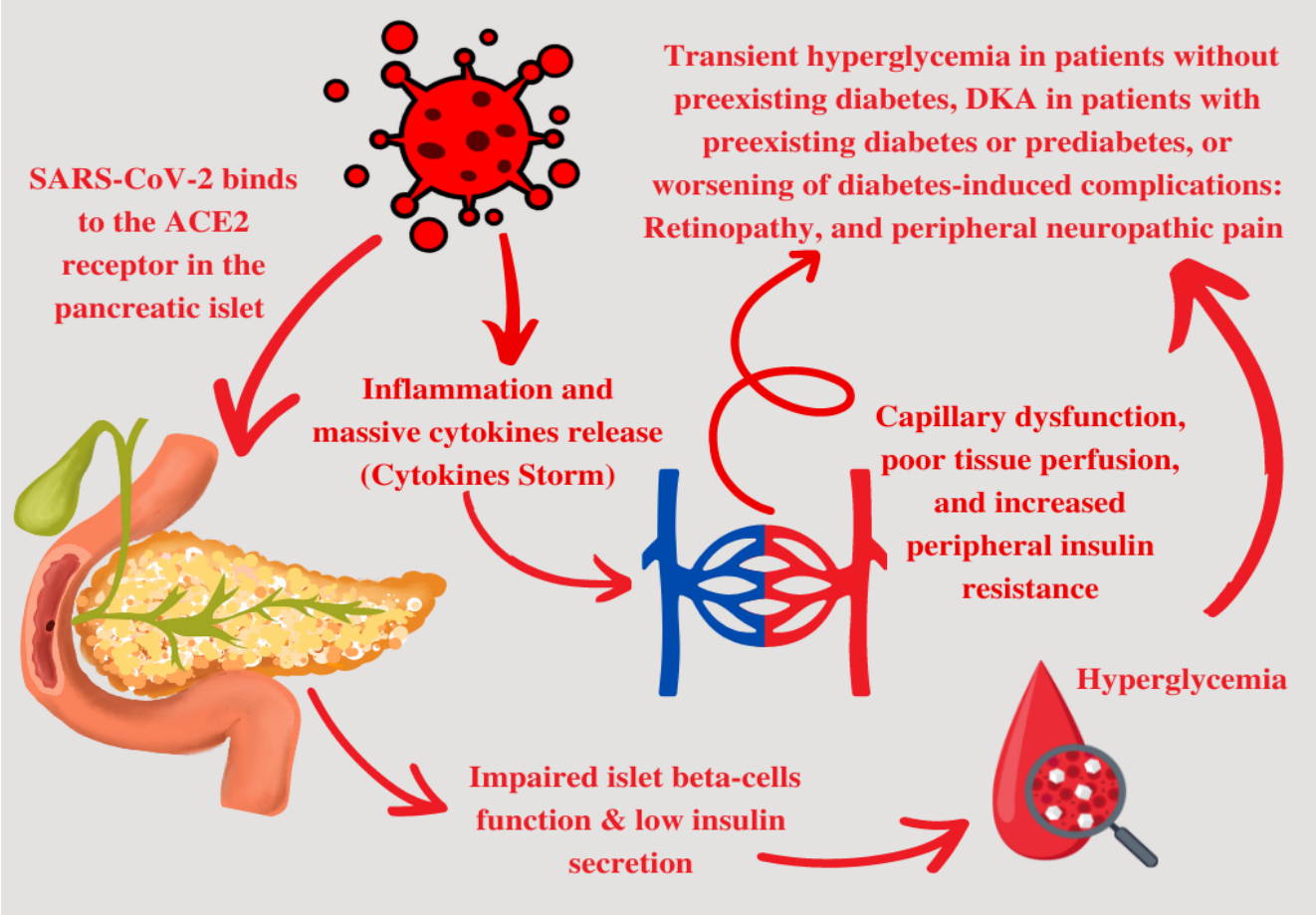
Discussion: It is well documented that an active COVID-19 illness can worsen diabetes. It is important to recognize that COVID-19's effect on diabetes may appear or persist for several weeks after recovery. Monitoring glycemic parameters during the 12-week time frame after COVID-19 illness may help identify these delayed effects. Identification of delayed onset or impact of COVID-19 illness on diabetes can help restore glycemic control and reduce morbidity.

INTRODUCTION

There is a bidirectional relationship between diabetes mellitus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) illness (COVID-19). Diabetes is a risk factor for severe COVID-19 illness. Conversely, worsening of pre-existing diabetes, including diabetic ketoacidosis (DKA), and new onset diabetes have been observed in patients with

COVID-19 illness.[1] The two cases presented here further highlight the relationship between COVID-19 illness and diabetes and introduce a delayed onset or impact aspect of this relationship. Both of these case reports describe the effect of COVID-19 on diabetes occurring weeks after recovering from COVID-19 illness. Our review of the literature did not produce a theory related to the delayed onset of effect of COVID-19 illness and negative diabetes outcomes. The SARS-CoV-2 virus is a fast, mutable virus. Its genome accesses human cells through cell surface receptors known as Angiotensin Converting Enzyme 2 (ACE2). This receptor is highly expressed in many organs including the lungs, brain, liver, kidneys, placenta, pancreas, gastrointestinal system, testes, and cardiovascular system.[2-5] The SARS-CoV-2 virus infects the pancreatic islet beta-cell through the ACE2 receptor, resulting in low insulin secretion manifesting as hyperglycemia. The increased release of pro-inflammatory cytokines, capillary dysfunction, and hyperglycemia due to COVID-19 illness can worsen glycemic control in individuals with diabetes, induce severe metabolic complications such as DKA, hyperosmolar hyperglycemic state, or peripheral neuropathic pain.[3-5] Figure 1 illustrates the relationship between the SARS-CoV-2 virus, COVID-19, and diabetes.

Figure 1. Relationship between SARS-CoV-2 and diabetes[3-5]



CASE PRESENTATION

Patient-A is a 28-year-old Hispanic male with a history of schizophrenia and substance use disorder in remission residing in a long-term psychiatric hospital. Past medical history included prediabetes, gastrointestinal reflux disease (GERD), hypothyroidism, hyperprolactinemia, borderline intellectual functioning, and vitamin D deficiency. Prediabetes was diagnosed in 2018, and he was prescribed metformin 500 mg by mouth twice daily, but it was discontinued in early 2020 to reduce pill burden, as his glycated hemoglobin (HbA1c) was below goal. In late 2020, Patient-A contracted COVID-19 illness. He was unvaccinated for COVID-19 at that time. During his mild illness, he required minimal medical attention other than over-the-counter medication management for symptoms (e.g., antipyretic, cough suppressant) and recovered fully without incident. Ten weeks after recovery from COVID-19 illness, he developed symptoms of recurrent headache, dizziness, and fatigue of 5-7-day duration, which led to an emergency department visit and medical hospitalization. He was diagnosed with DKA. His HbA1c was 11.6%. The DKA resolved after fluid resuscitation, potassium supplementation, and continuous insulin infusion. He was discharged back to the psychiatric hospital 9 days later. He was discharged on the following medications: insulin glargine 80 units subcutaneous injection every morning, and insulin lispro 26 units subcutaneous injection three times a day before meals. Comparing his glycemic control four months prior to COVID-19 illness and the DKA presentation, his fasting blood glucose was 120 mg/dL and HbA1c was 5.6%. At a 2-week follow-up appointment after discharge from hospitalization for DKA, Patient-A was restarted on metformin and titrated to a dose of 1000 mg by mouth twice daily along with his insulin regimen for better glycemic control. All insulin therapy was discontinued approximately 1 year after hospitalization for DKA, and his HbA1c was 6.3% at that time. His antipsychotic treatment for schizophrenia, olanzapine, remained unchanged during this entire time frame.

Patient-B is a 63-year-old white male with a history of schizoaffective disorder and stimulant use disorder in remission residing in a long-term psychiatric hospital. Past medical history included type 2 diabetes mellitus, GERD, vitamin D deficiency, and iron deficiency anemia. His glycemic control medication at this time was metformin ER 2000 mg by mouth daily. In late 2020, Patient-B contracted COVID-19 illness. His vaccine status for COVID-19 was unknown. During his mild illness, he required minimal medical attention other than over-the-counter medication management for symptoms (e.g. antipyretic, cough suppressant) and recovered fully without incident. Approximately one month after recovery from COVID-19 illness, Patient-B complained of significant foot pain including a slow healing wound and was transferred to a medical hospital. Osteomyelitis was ruled out as a cause of his pain. He received wound care and was discharged back to the psychiatric hospital. Approximately 2 months after recovery from COVID-19 illness, his fasting blood glucose was 265 mg/dL and his HbA1c was 10.3%. Comparing his glycemic control one month prior to COVID-19 illness, his fasting blood glucose was 174 mg/dL and HbA1c was 7.5%. His glycemic control regimen was adjusted to sitagliptin 50 mg by mouth once daily, insulin glargine 20 units subcutaneous injection daily, insulin lispro 10 units subcutaneous injection three times a day before meals, and continuation of metformin. Additionally, he was diagnosed with diabetes-induced peripheral neuropathy and started on gabapentin 100 mg by mouth three

times a day. His antipsychotic treatment for schizoaffective disorder, paliperidone palmitate long-acting injectable, remained unchanged during this entire time frame.

DISCUSSION

These two cases illustrate the negative effects of COVID-19 illness on diabetes and provide additional evidence for this relationship. Other reports of COVID-19 illness worsening glycemic control or causing serious acute metabolic complications such as DKA occurred simultaneously with or during the COVID-19 illness.[1] Worsening of diabetes in our cases presented with a delayed onset following full recovery from mild COVID-19 illness. The two patients were residing in an inpatient psychiatric hospital, so confounding factors that can worsen diabetes, such as medication nonadherence and significant changes in diet and exercise, are unlikely contributors to the worsening of their diabetes. Psychiatric medications, especially second-generation antipsychotics (SGA), are known to cause metabolic side effects. Although both patients were taking SGA, there were no changes in their psychiatric medication regimen, and they had been treated with these medications for a substantial period of time (i.e. > 1 year) prior to COVID-19 illness.

A literature review was conducted using PubMed database and the following keywords: SARS-CoV-2, diabetes mellitus, COVID-19, hyperglycemia, and diabetic ketoacidosis. The search was limited to articles published in English, and all pertinent literature was reviewed for inclusion.

There were reports from China, Italy, and Germany at the beginning of the pandemic of DKA and new onset of type 1 diabetes mellitus associated with COVID-19 illness.[1] A study conducted by Li et al. examined 658 hospitalized patients with COVID-19 illness in China and found 6.4% had ketosis at admission. Only 15 of these 42 patients had a confirmed history of diabetes. In this same study, 5 patients developed delayed ketosis with 2 of these 5 patients having no previous diagnosis of diabetes.[6] This study provided evidence that COVID-19 illness can cause diabetic and nondiabetic ketosis at an early or delayed onset, but delayed onset is significantly less common. Our cases add to the small body of literature associating COVID-19 with delayed onset metabolic adverse events.

CONCLUSION

COVID-19 illness can worsen glycemic control and induce diabetes-related complications such as DKA in patients with diabetes. It is important to recognize that the effect of COVID-19 illness on individuals with diabetes can have a delayed onset or persist for several weeks following recovery from the illness. More intensive monitoring of glycemic parameters during the 12-week time frame after recovery from COVID-19 illness may help identify these delayed metabolic adverse effects and reduce morbidity.

Notes
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